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REDAKSIONEEL · EDITORIAL

AKUTE ASEMHALINGSVERSAKING

VORDERINGS IN DIE DIAGNOSE EN BEHANDELING DAARVAN

Die referaat deur Elliott, Kamener, Zwi *et al.* wat elders in hierdie uitgawe gepubliseer word, bevat 'n belangrike ontleding van die meganisme en die manifestasies van akute asemhalingsversaking. Die skrywers benader die probleem uit die standpunt van die fundamentele fisiologiese beginsels wat daarby betrokke is. Die resultaat is nie alleen 'n bydrae tot ons begrip van asemhalingsfisiologie nie, maar ook 'n demonstrasie van die noodsaaklikheid vir 'n algehele herorientering van ons houding teenoor die volgende probleme: wat asemhalingsversaking eintlik is, hoe dit herken, en hoe dit behandel moet word. In laasgenoemde opsig dui die skrywers nuwerwetse tegnieke aan wat verreikende reperkussies op verpleegtoestande in gewone sowel as operasiesale kan hê.

Die gewilde begrip dat suurstof die wondermiddel vir die behandeling van asemhalingsversaking is, sal beslis gewysig en miskien heeltemal laat vaar moet word. Wanneer die probleem fisiologies ontleed word, moet sekere faktore geëvalueer word in die lig van die rol wat hulle speel in die veranderde toestande wat akute asemhalingsversaking vergesel, bv.:

(*a*) Die volume lug wat uitgeasem word;
(*b*) die koolstofdioksied-inhoud van die bloed en die uitgeasemde lug;
(*c*) Water- en hitte-verlies.

Die belangrikheid van die volume lug wat geasem word, kan nie te veel benadruk word nie. In gevalle van versaking waar 'n verhoogde minuut-volume noodsaaklik is om die

ACUTE RESPIRATORY FAILURE

ADVANCES IN ITS DIAGNOSIS AND MANAGEMENT

The paper by Elliott, Kamener, Zwi *et al.*, which we publish elsewhere in this issue, comprises an important analysis of the mechanism and the manifestations of acute respiratory failure. The authors have approached the problem from the standpoint of the fundamental physiological principles involved. The result is not only a contribution to our understanding of respiratory physiology, but also demonstrates the need for a total reorientation of our attitude to what constitutes respiratory failure, how it is to be recognized and how it is to be treated. In the latter respect the authors have indicated novel techniques which will have far-reaching repercussions on the conditions of nursing in the ward as well as in the operating theatre.

The popular concept that oxygen is a panacea for the treatment of respiratory failure certainly needs to be modified, if not abandoned. When the problem is analysed physiologically, certain factors must be evaluated for their roles in the altered conditions which obtain in acute respiratory failure, e.g.:

(*a*) The volume of air respired;
(*b*) The carbon dioxide content of the blood and the respired air;
(*c*) Water and heat loss.

The importance of the volume of air breathed cannot be overemphasized. In failure, when an increased minute volume is essential for remedying the situation, the authors have demonstrated the urgency and the value of tracheotomy as a medical (rather than a sur-

toestand te bestry, wys die skrywers op die dringendheid en die waarde van tracheotomie as 'n mediese (liewer as 'n chirurgiese) maatreël, veral in die afwesigheid van 'n meganiese obstruksie van die lugweë. Die resultaat is 'n onmiddellike vermindering van die dooie ruimte, 'n verhoogde minuut-volume, en 'n kleiner las vir die asemhalingspiere. Dit kos die pasiënt minder om meer asem te haal. Die skrywers beskou hierdie stap trouens as so belangrik en lewensreddend dat hulle die volgende slagspreuk gesmee het: ‚As u twyfel, doen 'n tracheotomie.'

Die rol van koolstofdioksied verg sorgvuldige evaluasie. Die praktisyn moet gedurig oppas dat hy nie iets wat in die eerste en vernaamste plaas 'n gebrek aan suurstof is vir koolstofdioksiednarkose aansien nie. Tracheotomie, wanneer dit aangedui word, sal veel tot die outomatiese herstel van hierdie deel van die versteuring bydra.

Wat water- en hitteverlies betref, sal die waarnemings van die Johannesburgse werkers seer sekerlik 'n belangrike invloed op die begrip en behandeling van akute asemhalingsversaking uitoefen. Hul werk beklemtoon dat noodlottige versteurings van die hitteregulering baie maklik kan voorkom, en dat 'n ramp met byna ewe groot gemak vermy kan word deur die toepassing van eenvoudige, helende maatreëls. Die seisoens- (d.w.s. somer-) voorkoms van asemhalingsversaking dui op die belangrikheid van omgewingstoestande. Die buitengewoon sonnige kant van 'n saal kan bv. rampspoedige gevolge vir die welsyn van kwesbare pasiënte meebring. 'n Hoë koors kan oor die hoof gesien word as die geneesheer hom bloot op mondtemperature verlaat. Die koorspennetjie moet in die rectum geplaas word. Die praktiese resultaat van hierdie waarnemings was die invoering van yswaterlawemente as 'n doeltreffende manier vir die vermindering van wat andersins onkeerbare en onbeheerbare hoë koors (met al die rampspoedige gevolge daarvan) kan word.

Die toepassing van hierdie belangrike waarnemings op die ontwerp en konstruksie van operasiesale is duidelik en ondubbelsinnig. Die eerste en vernaamste vereiste is operasiesale met doeltreffende lugreëling wat chirurgie geriefliker vir die chirurg en veiliger vir die pasiënt sal maak.

Die reperkussies op verpleegtegnieke is ook aansienlik, en die noodsaaklikheid vir onmiddellike wysigings in die leerplanne van studente in alle vertakkinge van die mediese praktyk is nou voor die hand liggend.

Vir moderne narkotiseurs sal dit van waarde wees om hierdie beginsels in hul narkosepraktyk te integreer. Trouens, Samson het onlangs in hierdie tydskrif aangetoon* dat 'n vermindering van die dooie

* Samson, H. H. (1960): Med. Bydr., **6**, 301.

gical) measure, particularly in the absence of mechanical obstruction to the air passages. The result is an immediate reduction in the dead space, an increased minute volume and a diminished burden on the respiratory muscles. It costs the patient less to breathe more. Indeed, the authors regard this manoeuvre as so valuable, in fact life-saving, that they have developed the maxim: 'When in doubt, do a tracheotomy.'

The role of carbon dioxide needs careful evaluation. The practitioner must constantly be on the alert not to mistake as carbon dioxide narcosis something which may really be primarily an oxygen lack. Tracheotomy, when indicated, will do much for the automatic restitution of this part of the derangement.

It is in connexion with water and heat loss that the observations reported by the Johannesburg workers will surely make their greatest impact on the understanding and the management of acute respiratory failure. Their work stresses the ease with which fatal derangements of thermal regulation may occur and the almost equal ease with which catastrophe may be averted by the employment of simple remedial measures. The seasonal (i.e. summer) incidence of respiratory failure pointed to the importance of environmental conditions. The unduly sunny side of a ward may, e.g. be disastrous for the welfare of vulnerable patients. Hyperpyrexia may go undetected if oral temperatures are relied on. The thermometer must be placed in the rectum. The practical result of these observations has been the introduction of ice water enemas as an effective way of reducing what may otherwise become an irreversible and uncontrollable hyperpyrexia with its disastrous outcome.

The application of these important observations to the design and construction of operating theatres is clear and unambiguous. The essential need is for air-conditioned theatres which will make surgery more comfortable for the surgeon and safer for the patient.

The repercussions on nursing techniques are also considerable, and the need for rapid adjustments in the curricula of students in all branches of medical practice is now obvious.

Modern anaesthetists will find it profitable to integrate these principles into their anaesthetic practice. Indeed, Samson has recently shown in this journal* that the reduction of the dead space to the physical minimum possible can to-day readily be achieved. This is a sound physiological approach which fits in well with the suggestions developed by Elliott, Kamener,

* Samson, H. H. (1960): Med. Proc., **6**, 301.

ruimte tot die fisies moontlike minimum vandag maklik bewerkstellig kan word. Dit is 'n gesonde fisiologiese benadering wat goed aanpas by die wenke wat deur Elliott, Kamener, Zwi *et al.* aan die hand gedoen word vir die nuwe toestande wat vir pasiënte sowel as dokters in operasiesale geskep behoort te word.

Die beklemtoning van temperatuurversteurings in die gevalle wat deur die skrywers beskryf word, skyn 'n pioniersontwikkeling te wees wat maklik toegepas behoort te kan word in die behandeling van die versteurde pasiënt, sowel as in profilakse. Van die uiterste belang is dat die praktisyn op hoogte moet wees van die maatstawwe vir die herkenning van asemhalingsversaking, die indikasies vir die behandeling daarvan, en die aanwending en toepassing van wat in sy wese 'n eenvoudige en tog lewensreddende tegniek is.

Zwi *et al.*, for the new conditions under which patient and doctor should function in operating theatres.

The emphasis on temperature derangement in the cases the authors have described appears to be a pioneering development which will have a ready application in the management of the disturbed patient as well as in prophylaxis. The important thing is for the practitioner to become aware of the criteria for recognizing respiratory failure, the indications for treating it as well as how to use what is an essentially simple (but life-saving) technique.

ABSTRACTS

KIDNEY TRANSPLANTATION FOR RENAL INSUFFICIENCY?

In the event of acute renal failure, various methods of treatment are available to-day, such as exsanguination transfusion, peritoneal dialysis and the artificial kidney. Although these techniques sometimes require complicated apparatus, they are nevertheless considerably simpler than renal transplantation. This method, however, would seem to be indicated for a chronic nephropathy which runs a severe course and in which the other procedures are of little use because they cannot be repeated often enough.

Renal transplantation involves technical and biological difficulties. The technical obstacles can be considered as overcome to-day because, thanks to the advances made in vascular surgery, it is possible to implant a kidney and provide it with an adequate blood supply. On the other hand, the biological problem of incompatibility has only been partially solved by the method of homeotransplantation. Renal transplantations between enzygotic twins have proved successful but, from the biological point of view, these are really autotransplantations.

Lefebvre holds the view that, at the present stage, homoeotransplantation is not indicated in cases of renal insufficiency. Apart from the difficulty of finding a suitable donor, the proportion of successful transplantations is less than 50%.

[Lefebvre, L. (1958): La transplantation rénale Rev. Méd. Liège, **13,** 95].

THE USE OF EXSANGUINATION-TRANSFUSIONS

Whereas the artificial kidney is indicated in cases of anuria without haemolysis or in protracted anuria of haemolytic origin, exsanguination-transfusion—provided it is used as soon as possible—is the specific therapy for severe haemolytic anuria. This method alone makes it possible to replace blood which has undergone pathological changes owing to the fact that its plasma is charged with haemolysing toxins, that dissolved haemoglobin has reached high levels, or that the erythrocytes have become particularly fragile.

The prognosis depends not only on the extent of the existing haemolysis but also on the speed with which therapeutic measures are taken and on the amount of blood transfused. At least 7 litres, preferably 8–10 litres, must be used. The transfusion should be repeated on the following day if there are still considerable quantities of dissolved haemoglobin in the blood. Where the exsanguination-transfusion is begun in the first 48 hours after the appearance of haemolysis, the chances of success seem to be considerably better than if the commencement of therapy is delayed. For instance, 5 of 17 patients suffering from anuria as a sequel to abortion could be saved by prompt treatment; of the other 12 patients, however, who did not receive an exsanguination-transfusion until 3–19 days after the abortion, 7 died. As a rule, a patient is given 3–5 transfusions, depending on the duration of the anuria and the degree of azotaemia.

[Milliez, P., Laroche, Cl. and Ky, N. T. (1955): Rev. Méd. Liège, **13,** 70].

A RHEUMATISM TEST

Inflammatory processes of rheumatic origin can be differentiated from those of other aetiology by inunction with Trafuril, a vasodilator. The 'normal' reaction to Trafuril consists in reddening of the skin, with or without swelling; it is found in healthy subjects and, for example, in tuberculosis patients. The reaction is 'abnormal' when there is no reddening, but even slight blanching, which usually suggests a rheumatic process. The Trafuril ointment—as well as a placebo ointment—was in each case applied to the volar aspect of the forearm.

The authors have extended their earlier tests on inflamed joints by studying inflammatory processes of all types in a series of 226 patients and 74 healthy subjects. They have confirmed their former results. Of 60 rheumatic patients, 87% had an abnormal reaction, while the response was abnormal in only 4.1% of 74 control subjects and in only 9.8% of 166 tuberculosis patients, of whom two thirds had received no isoniazide. An unexpected result was that those tuberculous patients who were treated with isoniazide showed the abnormal reaction only half as often as the average for the tuberculosis cases. This cannot be explained. Perhaps there are differences in the metabolism of the nicotinic acid derivatives, involving also the catabolism of tryptophane.

[Saslaw, M. S. and Streitfeld, M. M. (1957): J. Florida Med. Assoc., **44,** 152].

ACUTE RESPIRATORY FAILURE AND ITS MANAGEMENT

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WITH THE TECHNICAL AND PROFESSIONAL ASSISTANCE AND COLLABORATION OF

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Respiratory insufficiency is a condition in which the lungs (because of defects in one or more of their functions of ventilation, diffusion and perfusion) cannot supply the oxygen demands of the body efficiently. When insufficiency results in arterial hypoxia, carbon dioxide retention and, occasionally, heat retention, *respiratory failure* is, by definition, present. These two conditions are not restricted to chest disease. Following surgery of the abdomen or after head injuries, patients may develop acute fulminating respiratory failure without primary pulmonary lesions.

This article is an analysis of the management of a group of patients who developed respiratory failure from a variety of causes. The use of antibiotics, bronchodilators, cortisone derivatives and digitalis will not be discussed. Consideration will be given to the procedures of oxygen administration, tracheotomy, the use of artificial respirators and the regulation of body temperature.

Proper use of these procedures may be life-saving. Improper use, which is not at all uncommon, may jeopardize the life of the patient still further. Maladministration of oxygen is common. Carbon dioxide narcosis is a dangerously frequent wrong diagnosis. Tracheotomy is often thought to be indicated only for laryngeal obstruction, but is of great value in other causes of respiratory difficulty. Artificial respirators are often not doing what their dials are believed to indicate; volume changes in the lung certainly cannot be directly inferred from the pressure changes on the dials. Dangerous hypopyrexia or hyperpyrexia not uncommonly accompanies crises of acute pulmonary insufficiency and can pass undiagnosed.

In the preface to a standard work on respiratory physiology Comroe[1] remarks:

'Pulmonary physiologists understand pulmonary physiology reasonably well. Many doctors and medical students do not. One reason is that most pulmonary physiologists, in their original and review articles, write for other pulmonary physiologists and not for doctors or medical students.'

This article is intended to show that a knowledge of simple principles of respiratory physiology is essential for the rational and proper treatment of pulmonary insufficiency, and that simple bedside observations are usually adequate in controlling such treatment.

GENERAL CONSIDERATIONS

Acute respiratory failure results when the regulation of oxygen, carbon dioxide and body temperature becomes defective.

The volume of air that enters the lung each minute (abbreviated as MV) is the standard of measurement of ventilation and is the product of the respiratory rate and the tidal volume, i.e. the volume of air inspired each breath.

A normal subject at our altitude of 6,000 feet above sea level has a minute resting ventilation of 6–11 litres, the volume varying with the size and constitution of the subject.[3] Ventilation normally results in a number of physiological consequences:

i. Oxygen is supplied to the body by the proportion of the oxygen of alveolar air that enters the pulmonary capillary blood. An increasing oxygen requirement is met by increasing the minute ventilation.

ii. Carbon dioxide is disposed of. An increase of carbon dioxide from any increase of metabolism, e.g. raised body temperature or the expenditure of muscular energy including the energy consumed in the process of ventilating, is met by increasing the minute ventilation.

iii. Body heat and body water are lost. The inspired air has a low temperature and a low water content. When it enters the lungs, it is warmed to the body temperature and saturated with water vapour. Significant amounts of body water and body heat are normally lost in this way.

iv. Energy is used in the process of breathing.

Hypoxia is the most important single feature of acute respiratory failure and may be contributed to by:

(*a*) *Hypoventilation.* Any deficiency in breathing may lead to decreased MV so that less air, and therefore less oxygen, enters the lung and becomes available for respiratory exchange. Also, less carbon dioxide is expelled and as this carbon dioxide accumulates, it encroaches upon the space available for oxygen. The movement of oxygen into the capillary blood from the alveolar air is normally much slower than the movement of carbon dioxide in the opposite direction. Retention of carbon dioxide reduces the affinity of haemoglobin for oxygen. For all these reasons, hypoventilation results in arterial oxygen desaturation.

(*b*) *Excessive Work of Breathing.* The act of ventilation is an energy-consuming process, the muscles of respiration themselves consuming oxygen.[2] The amount of oxygen consumed by the respiratory muscles is normally small in the resting subject but becomes important when large volumes of air are passing in and out of the lungs. Thus, when the normal subject breathes at his maximum rate (a procedure which can be maintained only for 15–30 seconds and which is termed the Maximum Breathing Capacity and is expressed in litres per minute) more oxygen is used by the muscles of breathing than by the rest of the body. Even at half the maximum breathing capacity most of the oxygen consumed by the normal subject is used by the muscles concerned in the process of breathing. In patients with chest diseases, where mechanical difficulty is encountered in breathing, the oxygen cost of the work of ventilating at rest may be considerable and become formidable on even slight exertion. The muscles of breathing not only use oxygen, but also produce carbon dioxide.

(*c*) *High Body Temperature.* Rise of body temperature causes disturbances which can impair the mechanism whereby oxygen passes readily from alveolar air into the pulmonary capillaries. At 98.4°F. (the normal body temperature) 6% of the alveolar air consists of water vapour. At 106°F. water vapour pressure increases so that it occupies 12% of the total alveolar air and encroaches upon the space for other gases, to the patient's disadvantage. At this temperature carbon dioxide is held less readily in the blood and is therefore given up freely into the alveolar air, further reducing the space available for oxygen. Furthermore, each degree Fahrenheit rise in temperature increases the body requirement of oxygen by at least 7%.

In acute respiratory failure, body temperature may be raised due to infection or to hypoventilation or to both. This is commonest during the hot season, in overheated wards in winter or in overheated operating theatres.

In some of our patients who were hyperventilating and were cyanosed, the expected reduction in minute ventilation or pulse rate after administration of oxygen did not occur. In these patients, hyperpyrexia (rectal temperature) was eventually found to be present. They were, in fact, over-breathing when they were hyperpyrexial in order to lose body heat. Why were they hyperpyrexial in the first instance?

The body normally produces about 100 Calories of heat per hour at rest (5 Calories for each litre of oxygen consumed), which is dissipated by a number of mechanisms. The skin is the most important heat regulating agent, as it provides a large surface from which radiation and evaporation may occur. Ventilation normally accounts for about 15% of the heat loss of the body by warming of inspired air to body temperature and, more important, by saturating the air with water vapour, each ml. of water lost by ventilation removing 0.58 Calories from the body. If heat loss from the body is prevented, the temperature will rise 2°F. for each Calorie that is retained per litre of body water.

The early experiments on heat loss were conducted on normal subjects exposed to relatively cool, dry, atmospheric conditions. The subjects were usually semi-nude, so that the greater portion of their total surface area was exposed to moving air. A patient encased in a metal tank respirator, to take an extreme case, presents a different problem of heat loss as he does not have the benefit of a large skin surface for evaporation and radiation. Mild dehydration and a moderate working load have been shown to induce pyrexia rapidly in the normal subject.[4, 5] Any sick person covered by blankets with only his head exposed to the atmosphere is without part of his heat losing mechanism, may be dehydrated, and may have to do an increased amount of metabolic work. If he does not hyperventilate adequately to lose heat he will become pyrexial, and if this pyrexia is not controlled, hyperpyrexia may develop extremely rapidly.

The oral temperature may often not reflect this rise, probably because the mouth, as in the dog, is part of the heat-losing system. The rise must be measured elsewhere. Measurement *per rectum,* in the oesophagus and sometimes even under the breast, is satisfactory. The discrepancy between oral and rectal temperature in these cases may be 5–8°F. This problem of hyperpyrexia associated with respiratory failure emergencies is common, and is often not recognized. The temperature may rise very rapidly, as much as 5°F. in one hour. The patient usually succumbs when his body temperature exceeds 108°F.

In pathological conditions of the lung there is a loss of lung tissue, and oxygen consumption can be maintained at a normal level only by an increase of the minute ventilation, which may be visible to the naked eye or measurable only by spirometry. This hyperventilation is present in any compensated pathological condition in which oxygen requirements are increased. As the capacity to hyperventilate compensatorily fails, the oxygen saturation of the arterial blood tends to fall and some degree of carbon dioxide retention occurs.

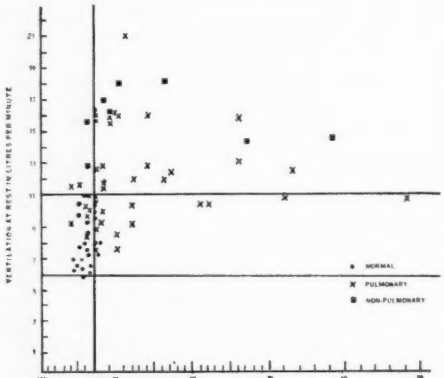


Fig. 1. Resting minute ventilation and arterial oxygen saturation in a group of normal subjects, patients with chest disease and other patients. Note that nearly all the patients show an increase in minute ventilation. This increase is less obvious in patients whose arterial oxygen saturation is low.

The importance of hyperventilation as a process of physiological adaptation to either lung pathology or to the increased oxygen requirement in other diseases, is demonstrated in Fig. 1. The resting Minute Volume of primary pulmonary cases, of non-pulmonary (cardiac) cases and of normal subjects is plotted against the resting arterial oxygen saturation. Many of the patients with pulmonary or cardiac disease have virtually normal arterial oxygen saturations, but have notable increases in minute ventilation, up to 16 litres per minute.

The patients with arterial oxygen saturations of less than 80% have relatively small minute volumes compared to the other patients, suggesting that hyperventilation is the way by which a patient with a reduction in pulmonary tissue or increased oxygen requirements can maintain a normal supply of oxygen.

Carbon dioxide is more readily diffusible than oxygen so that a patient disposes of it more easily than he takes up oxygen. Compensatory hyperventilation to satisfy oxygen demands may therefore not unexpectedly cause a respiratory alkalosis (due to excessive loss of carbon dioxide) and the symptoms that go with it.

Carbon dioxide retention is next most important to hypoxia as an effect of respiratory failure.

Carbon dioxide in its own right, when retained, may cause metabolic difficulties. If the arterial blood concentration of carbon dioxide increases threefold, so that it exerts a pressure of 100 mm. Hg (normal CO_2 pressure = 35–40 mm. Hg) it acts as a depressant of nervous and muscular function, causing stupor and coma; CO_2 narcosis is dealt with in greater detail in a later paragraph.

If, on the other hand, the blood concentration of carbon dioxide is very low, the affinity of haemoglobin for oxygen is enhanced to such an extent that oxygen may not be given up to the tissues, and oxyhaemoglobin traverses the body without giving up the required oxygen. This situation is encountered mainly in patients who, during artificial respiration, lose large amounts of carbon dioxide by mechanical overventilation. The effect of a low body temperature also enhances the affinity of haemoglobin for oxygen. If hypocapnia and hypopyrexia coexist, haemoglobin is doubly reluctant to give up its oxygen.

In acute respiratory failure the 'dead space' of the respiratory system demands attention. The anatomical dead space is the volume of the conducting airways from the mouth and nose to the alveoli, in which no rapid exchange of oxygen and CO_2 takes place. This anatomical dead space may be added to by the tubes of resuscitative equipment and the re-breathing bag of the oxygen mask. Alveoli with no capillary flow around them also contribute to dead space. In normal lungs this factor is insignificant; in emphysema it becomes important. The greater the dead space, the greater is

the energy expended (and therefore the oxygen cost) to pass a given quantity of air to and from the alveoli.

Hypopyrexia may be a feature of cases of acute respiratory failure who have been overventilated in tank respirators. This phenomenon will be considered in a later section.

The sequence of events in cases of acute respiratory failure in terms of minute ventilation volume, oxygen saturation, carbon dioxide content of blood, rectal temperature, heart rate and what, in our experience, was found to be the 'common erroneous diagnosis' is illustrated in Table 1.

TABLE 1: SEQUENCE OF EVENTS IN CASES OF ACUTE RESPIRATORY FAILURE. AS OXYGEN SATURATION DECREASES AND HEART RATE INCREASES, EITHER THE PICTURE OF ADVANCING CARBON DIOXIDE RETENTION OR OF INCREASING BODY TEMPERATURE, OR OF BOTH, DEVELOPS

Minute Ventilation (Litres per Minute)		*Oxygen Saturation*	*Heart Rate*	*CO_2 Content of Blood*	*Rectal Temperature*	*Common Erroneous Diagnosis*
Normal Finding	6–11	94%	90	Normal	Normal	
Compensated State	20	90%	120	Decreased	Normal	'Psychogenic hyperventilation.'
Early Uncompensated State	15	85%	140	CO_2 retention	Rising	'Impending Collapse.'
Late Uncompensated state. Pre-Terminal	8	70% to 80%	160	Acidosis from uncompensated CO_2 retention	Greater than 105° F.	'Collapse.'

It is seen that increasing grades of acute respiratory insufficiency were erroneously diagnosed as 'psychogenic hyperventilation,' 'impending collapse' and, finally, 'collapse.' Hypoxia is always present and is complicated either by hyperpyrexia or acidosis or both. Treatment for collapse, both in principle and in practice, is usually of no avail in such cases.

THE ASSESSMENT OF THE STATE OF RESPIRATORY FUNCTION IN REGARD TO TREATMENT

It is not necessary to be familiar with a battery of laboratory pulmonary function tests in order to understand the management of cases of acute respiratory failure. Simple bedside observations are often all that are necessary.

In making these observations, it is advisable that the patient should rest at a fixed angle of about 45°, since postural changes in themselves affect the respiratory rate. Forty-five degrees is comfortable and allows easy observation of neck and chest. These observations include the pulse rate, respiratory rate, blood pressure, colour (including the colour of the blood obtained from pricking a warm ear lobe), mental condition and temperature measured rectally. The frequency of observations will vary for each case. From a record of these signs at regular intervals, it is possible invariably to judge if the patient's respiratory function is unchanged, improving or worsening. His changing therapeutic requirements can be determined with objectivity as they arise, and the effect of resuscitative procedures is manifest from these simple observations almost immediately. For example, response of hypoxia to oxygen administration will be manifest in minutes. Tracheotomy, referred to in greater detail later, will improve the patient within the same period of time unless carbon dioxide retention is severe, when 20 minutes may be necessary before improvement can be noticed.

A 50% increase in pulse and respiratory rates, despite apparent well-being of the patient and even in the absence of central cyanosis, must be regarded as an indication for oxygen therapy.

It is well known that a patient's oxygen consumption may increase threefold or more, without the patient noticing any discomfort. This may be associated with an increase in respiratory rate to about 36, and an increase of pulse rate to at least 110 per minute. By the time the patient is conscious of his hyperventilation, i.e. when he is dyspnoeic, his pulse rate may be as high as 140, and his respiratory rate 40 to 50 per minute.

The assessment of cyanosis is usually regarded as a crude inaccurate sign. We have found it of great value. If there is uncertainty from clinical observation, the ear lobe is warmed for one minute with a moist swab at or just above body temperature, and its colour is observed. If there is still any doubt about the presence or absence of cyanosis, the ear is pricked so that a brisk flow of blood appears and the colour of the blood is noted. Cyanosed blood soon becomes pink on exposure to air, so that the assessment of the colour must be made immediately after the blood appears.

The presence or absence of cyanosis leads to important inferences. In general the presence of cyanosis is always an indication for oxygen. If the patient is breathing room air and is not cyanosed, it can be inferred that his ventilation is adequate for both oxygenation and removal of carbon dioxide and there is no danger of carbon dioxide narcosis. He may, however, be using excessive energy because of his compensatory hyperventilation. This wastage of energy may be avoided and clinical benefit become manifest by enriching his air intake with oxygen. When oxygen is administered, absence of cyanosis may rarely *not* imply an adequate removal of carbon dioxide, and carbon dioxide narcosis may be the cause if the condition deteriorates.

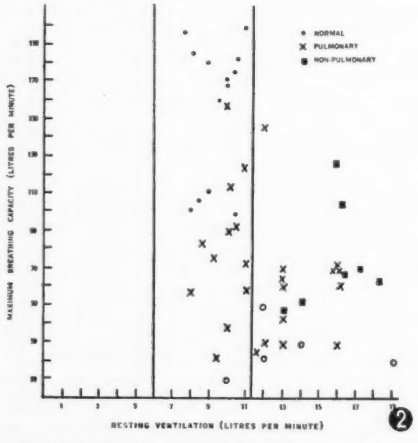
If the condition deteriorates in spite of the *adequate* administration of oxygen, assistance to respiration in the form of tracheotomy should be given and, if this fails, a respirator must be instituted.

The technical aspects of these procedures are dealt with later.

The measurement by portable gasometer or spirometer, of the volume of air ventilated per minute may be of value and even essential in certain cases. For example, the ventilation of patients in tank respirators is particularly difficult to judge visually, and bears little relationship to the dial pressure readings and the apparent movements of the chest wall. A gasometer or spirometer is essential to show whether a chest wall that 'moves' in the inspiratory and expiratory phases of the respirator is or is not ventilating the lungs.

The Maximum Breathing Capacity (MBC) defined in an earlier paragraph, may be of considerable value if the patient is fit enough to cooperate. The MBC provides information about the ability of the chest muscles to draw air in and out of the lung against the resistance offered by the air passages, the elasticity of the lung, the chest cage and the abdominal contents.

An arbitrary but clinically satisfactory estimate of the respiratory 'reserve' may be obtained from the ratio MBC : MV. This ratio is normally 20 : 1, the average values of MBC and MV being 160 and 8 litres a minute respectively. This ratio may be grossly reduced in acute respiratory failure due to an increase in MV and a decrease in MBC, as illustrated in Fig. 2. When the reserve ratio is greater than 4 : 1 there is no immediate danger to the patient. As the reserve ratio decreases to 2 : 1 respiratory failure is imminent.



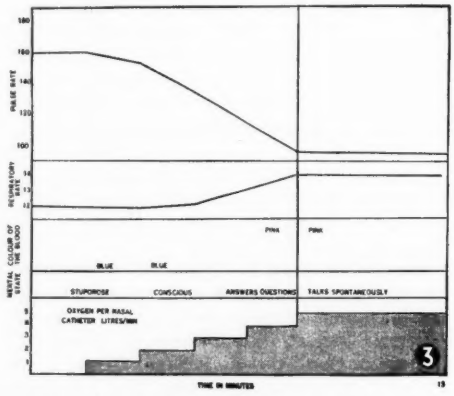


Fig. 2. The respiratory reserve is the ratio of the maximum breathing capacity to the resting ventilation. Note the decreased reserve of the patients. Five patients who required tracheotomies had reserves in the region of 2 : 1. They are indicated by open circles on the diagram.

Fig. 3. The administration of oxygen to a cyanosed patient by nasal catheter. The rapidity of response is illustrated.

The examination of the arterial oxygen, carbon dioxide and pH may be essential for the proper management of some cases. Examples are given in the next section, with an account of normal and abnormal values and their significance in the footnote.

Lastly, there are certain factors that enable one to anticipate in a particular case that respiratory insufficiency and failure may develop.

Obese subjects are particularly prone to acute respiratory failure. They have small lungs that are disposed to hypoventilate and predisposed to pneumonia and atelectasis. The weight of abdominal fat adds greatly to the pressure required for artificial respiration, a pressure high enough to have adverse effects on the pulmonary capillary circulation. Bronchitic, asthmatic and emphysematous subjects are predisposed on account of hypoventilatory and obstructive factors. Dehydration is notably contributory and must be rectified. A hot humid atmosphere is contributory, perhaps the commonest threat in this regard being the overheated operating theatre that is not air-conditioned.

CLINICAL PROBLEMS AND DIFFICULTIES ASSOCIATED WITH THE MANAGEMENT OF ACUTE RESPIRATORY INSUFFICIENCY OR FAILURE

THE EFFECT OF OXYGEN ON VENTILATION

The administration of oxygen causes a decrease in the minute ventilation in normal subjects, as well as in patients with mild respiratory pathology. Occasionally this reduction in minute ventilation may cause severe carbon dioxide retention.[6] This is uncommon. Usually the decrease in minute ventilation is associated with less work of breathing and less carbon dioxide production, so that the alveolar concentration of carbon dioxide either decreases or remains unchanged.[7-9] Patients with chest disease severe enough to cause hypoventilation and cyanosis usually increase their minute ventilation when given oxygen. Fig. 3 shows this response to oxygen in a 65-year-old male patient who had been admitted to hospital with emphysema and bronchopneumonia. He had received antibiotics but did not improve until 12 hours later, when he was given oxygen by nasal catheter. His rapid improvement is reflected in the change in his mental state and in the reduction in pulse rate. The slight but definite increase in respiratory rate after oxygen administration has been observed in a number of other patients presenting similar clinical problems. It would appear that the administration of oxygen in such cases makes the work of breathing more economical in so far as the rest of the body receives the benefit of the additional oxygen consumed.

HYPOVENTILATION WITH CARBON DIOXIDE RETENTION

Under-breathing from any cause results in carbon dioxide retention. This is illustrated by the following case of status asthmaticus.

A 43-year-old male with a 30-year history of asthma had been in status asthmaticus for 7 days. During this period he had failed to respond to treatment with aminophylline, adrenaline, antibiotics, hydrocortisone, oxygen and sedatives. On the seventh day he was found stuporose, cyanosed and clinically hypoventilating. His MV was 3 litres instead of the normal expected 9 litres per minute. His immediate deterioration had wrongly been attributed to sedation and oxygen therapy. His own ventilation while breathing air, or even pure oxygen, could provide him with a small fraction only of his normal oxygen requirement at rest. He was acidotic with an arterial pH of 7.25. His carbon dioxide combining power was at the upper limit of normal, being 27 mEq/L., indicating that he was not retaining sodium bicarbonate adequately to buffer the CO_2 that was being retained. The oxygen saturation estimated by the colour of warm earlobe blood was grossly reduced. He was in congestive cardiac failure with a pulse rate of 140 per minute and a blood pressure of 100/80 mm. Hg.

Oxygen was then administered through a mask and re-breathing bag, and artificial respiration instituted using a negative and positive tank-type respirator. The speed of the respirator was adjusted to the patient's respiratory rate of 10 breaths per minute and the negative and positive pressure was gradually increased. When the negative pressure was 14 cm. H_2O, his minute ventilation had increased only to 4.5 litres. Increasing the pressure exerted by the machine on his chest did not improve his Minute Ventilation further. The patient's mental condition was unchanged but his heart rate dropped to 100 per minute, and signs of congestive cardiac failure disappeared. His oxygen demands were being fulfilled, in spite of the low MV, but only because he was breathing supplementary pure oxygen. Carbon dioxide was not being expelled adequately by the procedures adopted so far.

After 24 hours of this regime his condition was unchanged. It was estimated that he had retained at least 200 ml. of carbon dioxide per minute. A carbon dioxide combining power of 33 mEq./L. indicated that CO_2 retention was being buffered to some extent, but the pH of the blood still revealed acidosis, being 7.23. As the volume breathed could not be increased by adjustment of the tank-type respirator, it was decided to make more effective use of what was being achieved by the respirator by administering oxygen by nasal catheter instead of by mask in order to reduce dead space (of the mask and the bag) and avoid re-breathing of carbon dioxide from the mask. Twenty minutes later the patient's mental alertness and pulse were considerably improved, and he was able to leave hospital a few days later fit for his normal occupational activity and golf.

This case was encountered early in our experience of respiratory failure. Our approach has since undergone modification in that oxygen in the first instance is given by nasal catheter, body temperature (rectal) if raised is reduced to normal, and if this procedure fails to cause the desired improvement a tracheotomy is performed. Artificial respiration can be given if necessary, using a positive pressure Radcliffe machine, but this is usually avoidable by the timely application of the forementioned procedures.

CARBON DIOXIDE NARCOSIS

Carbon dioxide narcosis is an uncommon condition in which gross accumulation of the CO_2 in the tissues, including the blood, causes uncompensated respiratory acidosis with severe depression of the tissue metabolism, presenting clinically as stupor and coma. Not only the absolute amount of CO_2 accumulation but also the rapidity with which the CO_2 accumulates determines the onset of clinical symptoms of the condition.

The usual cause is hypoventilation. Because it is commonly associated with hypoxia, it is confused with that condition, and its descriptions are confused still further by the number of ways in which CO_2 accumulation in the blood can be quantitated and recorded.* In a severe case of respiratory acidosis with CO_2 narcosis the raised arterial plasma CO_2 concentration may be variously (and therefore confusingly) expressed in terms of CO_2 pressure, of CO_2 content or combining power of plasma in volumes per cent, or in mEq. HCO_3 per litre. Representative figures for severe respiratory acidosis would be a pCO_2 of 100 mm. Hg, plasma CO_2 content of 100 volumes per cent, which is the same as 45 mEq./L (see *Footnote* for calculation), or a CO_2 combining power of 100 volumes per cent, which is also the same as 45 mEq./L. For practical purposes, plasma CO_2 content and combining power are the same. The pH in CO_2 narcosis must always be acid down to 7.2, which is the lowest figure compatible with life.

In the last 20 cases of respiratory failure referred to us with the provisional diagnosis of carbon dioxide narcosis, the condition was actually present in only 5. In one of these, carbon dioxide narcosis was due to carbogen having been used, and in 4 the condition was caused by the use of a mask and re-breathing bag and was cured within a few minutes by changing to oxygen administration by nasal catheter.

The mask and re-breathing bag requires care for its proper use. Hugh-Jones[10] states:

> 'It is essential that a good fit be obtained and the flow of oxygen from the cylinder be adjusted until the reservoir bag distends fully at the start of exhalation and remains half-full at the end of inspiration. Usually a flow of about 6 litres per minute is required for this, but either the flow must be increased or the fit of the mask improved until these conditions are achieved. Otherwise this mask simply acts as a re-breathing bag and increases the patient's carbon dioxide (which may already be excessive) without adding significant oxygen.'

In the remaining 15 cases, the true diagnosis was hypoxia due to various causes. In 5 the oxygen cylinder was empty, in 4 there was a faulty reducing valve and flow-meter; in 4 there was a leak in the circuit, and in 2 an oxygen tent was being used ineffectively. All responded favourably within 3 minutes to oxygen administration by nasal catheter.

Carbon dioxide narcosis may occur when there is hypoventilation or when there is an undue amount of dead space. The commonest cause of added dead space in our experience was the mask and re-breathing bag, but other causes were encountered.

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* The concentration of CO_2 in the blood can be measured either as gaseous CO_2 or as dissolved CO_2. Gaseous CO_2 in the blood is expressed quantitatively as a pressure in mm. Hg, the normal range of 'pCO_2' being 35–40 mm. Hg for arterial blood and 40–44 mm. Hg for venous blood. Dissolved CO_2 is expressed as a concentration per unit volume of whole blood or plasma. In relation to pulmonary function only arterial concentrations of CO_2 (and O_2) are of concern, for they reflect the efficiency of the process of arterialization of venous blood in the lungs and, furthermore, it is customary for certain valid practical reasons to refer to plasma, not to whole blood concentrations.

HYPERVENTILATION AS A CAUSE OF EXCESSIVE CARBON DIOXIDE LOSS

The hyperventilation of aspirin poisoning causes hypocapnia which is responsible for many of the symptoms of this form of poisoning. These symptoms can be treated effectively in adults by merely allowing the patient to re-breathe the expired air from a mask and re-breathing bag. The hyperventilation due to the aspirin effect usually persists, but the patient is considerably relieved symptomatically within 5 minutes. This form of symptomatic treatment is given in addition to the conventional treatment of aspirin poisoning.

Artificial respiration is the commonest cause of serious hypocapnia. The resultant alkalosis may cause the association of haemoglobin and oxygen to be relatively fixed so that the tissues can use only a small portion of the oxygen available in circulating oxyhaemoglobin. The high oxygen saturation of the arterial blood may disguise the fact that the tissues are severely hypoxic. Hypopyrexia, referred to in the next paragraph, has a similar inhibiting effect on oxygen-haemoglobin dissociation.

HYPOPYREXIA

Low body temperature may be a feature of respiratory failure treated by the artificial respirator.

The concentration of dissolved CO_2 was formerly expressed in 'CO_2 volumes per cent. of whole blood or plasma' and many textbooks still use this terminology. It is more rational, in view of the importance of CO_2 concentrations in the maintenance of acid-base equilibrium, to express the concentration in milligram equivalents (mEq.) per litre. The latter notation is calculated by dividing 'volumes of CO_2 per cent. of plasma (or whole blood)' by the factor 2.23. The concentration of CO_2 dissolved in H_2CO_3 can also be expressed in mEq. per litre and is calculated by multiplying the pressure in mm. Hg of CO_2 in alveolar air (which is readily measurable) by the factor 0.03.

Normal values for arterial plasma CO_2 at our altitude of 6,000 feet are:

	Volumes %	*mEq./L.*
(*a*) CO_2 content of plasma (H_2CO_3 + buffer HCO_3)	47–62	21–28 (mean 24)
(*b*) CO_2 'combining power' (buffer HCO_3 alone)	45–60	20–27 (mean 23)
(*c*) CO_2 dissolved plasma as H_2CO_3 ($=(a)-(b)$) ...	2.7	1.20
(*d*) CO_2 plasma pressure (pCO_2)	35–40 mm. Hg.	

'Buffer' HCO_3 ($BHCO_3$) consists mainly of $NaHCO_3$. It is the medium whereby trends of pH of the blood towards alkalinity or acidity are compensated by buffer action in order to maintain a normal pH of 7.4.

pH, measurable by the pH meter, is dependent upon the ratio $BHCO_3 : H_2CO_3$ (normally 20 : 1) and not on the absolute amounts of $BHCO_3$ or H_2CO_3. The normal arterial pH is 7.4. A pH below 7.4 (limit of survival 7.2) is the only *single* measure of acidosis, and a pH over 7.4 (limit of survival 7.6) the only *single* measure of alkalosis. Without a knowledge of the measure of pH, acidosis or alkalosis can be *inferred* if the CO_2 combining power is estimated (a simple laboratory technique) and considered in relation to the clinical state. Thus, a raised CO_2 content of blood occurs in respiratory acidosis, whereas in metabolic acidosis the CO_2 content is reduced. A raised plasma CO_2 in a case of respiratory failure due to emphysema indicates respiratory acidosis. A lowered plasma CO_2 in a case of diabetic ketosis indicates a metabolic acidosis.

'Compensated' acidosis or alkalosis, respiratory or metabolic, is said to be present when the pH is maintained normal due to successful buffering and other compensatory mechanisms. But there are in such cases measurable abnormalities of blood CO_2, blood base and other substances.

The term 'alkali reserve' requires definition in the context of respiratory failure. It is a figure representing the 'capacity' of the plasma (not whole blood) to hold CO_2. It is estimated by placing plasma in an atmosphere of CO_2 at 40 mm. Hg (which is the partial pressure of CO_2 in alveolar air) and, after equilibrium has been achieved at a standard pressure and temperature, the CO_2 content of the plasma is measured. The normal value for this 'total plasma CO_2 capacity' is 53–68 volumes per cent. The physically dissolved fraction of this total amount of CO_2 is known as the 'free capacity' (normal range 2.4–3.4 volumes per cent.), and the ionically combined fraction (normal range 50–65 volumes per cent., or (translated into mEq.) 22–30 mEq./L. HCO_3) is known as the 'alkali reserve'. The alkali reserve is mainly combined as bicarbonate, and is consequently sometimes confusingly referred to as 'bicarbonate CO_2'.

A premature infant underwent surgery for a tracheo-oesophageal fistula and failed to breathe when the chest was closed. He received artificial respiration from an adult-size positive-pressure Radcliffe respirator, attached to an endotracheal tube. As the dead space of the respirator was 50 ml. and the normal tidal ventilation of an infant is at the most 10–20 ml., the respirator pumped the expired air back into the infant's lungs, thus effectively preventing the loss of carbon dioxide. A severe acidosis resulted, recovery from which was irreversible by the time the patient was seen.

Another cause of CO_2 narcosis was encountered in a child who became apnoeic following status epilepticus. He received artificial respiration from a Boyle's anaesthetic machine. A soda lime canister for absorbing carbon dioxide had been omitted from the circuit, and the respiratory valve of the machine had an extremely high resistance which resulted in the expired air entering the bag of the machine instead of escaping into the atmosphere; it was therefore re-breathed. Death occurred due to carbon dioxide narcosis 2 hours later. Both cases were extremely ill and would certainly have died if they had not been artificially ventilated, but the method of artificial respiration applied was clearly not the optimum method.

A 20-year-old woman was admitted following a serious head injury. A few episodes of apnoea each lasting a few seconds preceded complete apnoea. Gross papilloedema was present, and the cerebrospinal fluid was haemorrhagic with a pressure of 300 mm. H_2O. Blood pressure was maintained by intravenous administration of noradrenaline.

In view of the severity of the injury, the neurosurgeon treating the patient suggested that 'hibernation' therapy be employed as favourable reports on this technique in serious head injuries had been published. The patient's temperature was therefore reduced by chlorpromazine and ice packs. One hour after admission the oral temperature was recorded as 94.5° F., which was the lowest point on the scale of the thermometer used. Her body seemed clinically to be much cooler than this, the condition being ascribed to shock.

Artificial respiration was administered because of the apnoea, by means of a tank respirator. From her body build, her normal resting ventilation was estimated to be about 7 litres per minute, but she was initially deliberately hyperventilated at 14 litres per minute to combat the acidosis that is generally associated with shock. The pH of the blood was not available at the time. After 30 minutes her ventilation was reduced to 7 litres per minute and her colour continued to be well maintained without oxygen administration. The pH of the blood was thereafter measured 8-hourly over the next 2 days, and showed a gross alkalosis. For this reason the minute ventilation was progressively decreased by the artificial respirator until after 36 hours it was less than 3 litres per minute.

It was realized at that point that her oxygen consumption and carbon dioxide production must each be about 6 litres an hour, which probably represented only 50% of her normal expected metabolism. Her Calorie production according to this estimate was no more than 30 calories each hour. During the period her minute ventilation was 7 litres her Calorie loss by means of breathing alone would have been about 40 calories each hour, so that more heat was leaving her body than was being produced. It seemed likely, therefore, that her temperature was lower than was being recorded and, on using a thermometer with a scale extending down to 80° F., her rectal and oral temperatures were found to be less than 85° F.

An attempt was made gradually to warm her, but she died several hours later from the cerebral injury which, in itself, it was appreciated, could have been the cause of the hypothermia. But cooling with ice packs and artificial hyperventilation *must* inevitably have contributed to hypothermia. Hypothermia of severe grade from whatever cause, probably cannot be tolerated for more than 48 hours;[11] ventilation will not occur spontaneously at this temperature, nor will oxygen dissociate adequately from haemoglobin. Over-ventilation by means of a respirator will cause alkalosis and this will also prevent the dissociation of oxygen from haemoglobin.

Two other examples of hypopyrexia were encountered who were being hyperventilated artificially, one a case of post-appendicectomy cardiac standstill, and one a case of head injury. Their body temperatures were lower than 94.5° F. and they were apparently acyanotic. But when a moist swab at 100° F. was applied to the ear lobe, the later became almost black in colour due to the oxygen dissociation that then occurred with the rise in temperature of ear lobe blood. This was evidence of the severe tissue hypoxia that was present due to the hypothermia, which was thereupon treated. The treatment of hypopyrexia of this origin is described in a later paragraph.

HYPERPYREXIA

Raised body temperature, as has been pointed out, is a common and important feature of respiratory failure. The temperature charts of 4 illustrative cases are shown in Fig. 4.

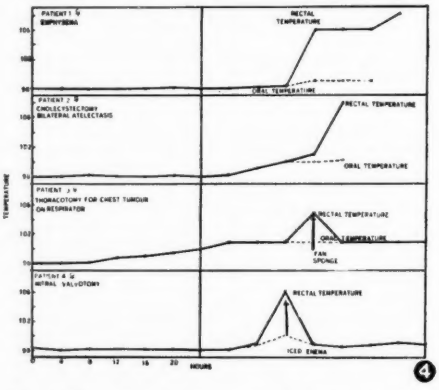

Fig. 4. Hyperpyrexia encountered in 4 patients with different chest conditions. All 4 began to deteriorate about 24 hours before hyperpyrexia was detected. At the time when the temperature was still normal, the skin was warm and there was increasing tachycardia and tachypnoea.
The first 2 patients were not effectively cooled and died with rectal temperatures of 108° F. The other 2 patients had the hyperpyrexia rapidly reduced by physical measures and survived.

The first patient was a 60-year-old woman who had been admitted because of increasing breathlessness. There was a 10-year history of bronchitis and she was polycythaemic with a haemoglobin of 24 g. %. She was treated with antibiotics, digitalis and diuretics.

A few days after admission she suddenly collapsed. She was then found to be cyanosed, the respiration rate was 36 and the heart rate was 130 per minute. She did not improve on oxygen administration by mask. Minute ventilation was above normal (20 litres) and the blood just alkalotic (pH 7.42). The heart rate increased to 170 beats per minute and her tachypnoea was sustained, a rather unusual finding in a patient with chronic obstructive chest disease.

Her skin initially felt extremely warm but both oral and rectal temperatures were normal. Deterioration continued and the arms became ice cold while the trunk remained hot to the touch. The oral temperature was unchanged, but her rectal temperature rose to 108°F. She died in this state about one hour after the sudden collapse. Necropsy revealed no cause of the hyperpyrexia.

The second patient underwent an uncomplicated cholecystectomy. The next day she began to show features exactly similar to those shown by the previous patient. Terminally her rectal temperature rose during one hour to 108°F., as did the axillary temperature, while the oral temperature was unchanged.

The significance of the hyperpyrexia as a problem requiring urgent treatment was not appreciated in these 2 cases.

A third patient, a 50-year-old woman, underwent thoracotomy for a tumour attached to the pericardium. Post-operatively the patient did not breathe spontaneously and a tracheotomy was performed. Artificial respiration was administered with a positive-pressure Radcliffe respirator. The Minute Ventilation was maintained at an abnormally low rate, with an oxygen supplement, because of certain adverse effects of the respirator on the pulmonary and systemic circulations, to which reference will be made later. Thirty-six hours later the heart rate increased from 120 to 150 beats per minute, her arms became ice cold but her trunk remained hot, and her rectal temperature rose within one hour from 100°F. to 105°F. This was treated immediately by fanning the patient and sponging her with cold water. The temperature returned to normal and she recovered.

A fourth patient, a woman of 30, had a repeat mitral valvotomy as an 'open heart' procedure. The day after the operation the heart and respiratory rates began to increase. The arms became cold, the rectal temperature rose to 106°F., the heart rate rose to 150, and the respiratory rate to 50 per minute. She became unconscious. Hyperpyrexia was treated with an enema of 250 ml. of cold tap water which contained small chips of ice that were just melting. Within 20 minutes she was conscious, the respiratory rate and heart rate improved considerably, and she recovered.

In all 4 cases, the oral temperature proved to be quite unreliable as a measure of the body temperature. The lack of reliability of an oral temperature reading in many cases has been reported elsewhere.[12] The suggestion[13] that bacterial activity in the rectum may be a factor in increasing rectal temperature, has no physical basis.

TECHNICAL ASPECTS OF THE TREATMENT OF ACUTE RESPIRATORY FAILURE

THE ADMINISTRATION OF OXYGEN

Oxygen may be administered in 3 different ways: by nasal catheter (short or nasopharyngeal), by mask and re-breathing bag, and by oxygen tent.

The normal MV of about 10 litres of air contains 2 litres of oxygen. This is diluted in the alveolar air which normally has an oxygen concentration of 14%.

A short nasal catheter provides an alveolar oxygen concentration of 30% and its only disadvantage is some slight and unimportant nasal irritation which is minimized by using gentle technique.

The longer naso-pharyngeal catheter provides an alveolar concentration of oxygen of 40–50%, but is likely to cause severe headaches.

The mask and re-breathing bag, properly used, gives an alvoeolar concentration of oxygen of 80%, but there is the risk of carbon dioxide retention, if special precautions, already mentioned, are not taken.

The oxygen tent gives an alveolar concentration of oxygen of 40%. The patient is not easily accessible for examination and special precautions are necessary to ensure temperature control in the tent and adequate flow-rate. The tent may be the only practical method of administering oxygen to children. The initial oxygen flow-rate must be at least 20 litres per minute, dropping later to 10 litres per minute.

We have found that, for practical purposes, short nasal catheters which just enter each nostril supported on Tudor Edwards spectacles, always supply enough oxygen for a patient at bed rest provided that he breathes more than 4 litres per minute. This technique is not only effective and more comfortable than the other techniques, but it is free from dangers, should the oxygen supply fail. Failure of the oxygen supply with the mask and re-breathing bag technique must complicate hypoxia with carbon dioxide retention; and similar dangers exist when an oxygen tent is being used. The nasal catheter technique permits the patient to be examined, to eat and to talk without interrupting the administration of oxygen.

This technique should effectively relieve cyanosis. If the cyanosis persists, the possibility

of a mechanical defect in the oxygen supply system and connexions must be looked for and corrected if present. Hyperpyrexia, right-to-left shunts in congenital heart disease, and the presence of abnormal haemoglobin pigments (e.g. methaemoglobin and sulphhaemoglobin) must also be considered. In all cases of cyanosis, except those due to abnormal haemoglobins, a sample of ear lobe or finger-prick blood exposed to the atmosphere rapidly becomes bright red.

TRACHEOTOMY

Tracheotomy may be of value in any case of respiratory failure and not only in laryngeal obstruction.

By excluding dead space from the larynx upwards, it immediately reduces the required tidal ventilation by 100 ml. per breath. At a respiratory rate of 20 breaths per minute this results in an immediate decrease in the minute ventilation of 2 litres without any reduction in the alveolar oxygen concentration. Ventilation is a mechanical action requiring energy, and its reduction by 2 litres in a patient in respiratory failure significantly reduces the oxygen cost of breathing. This may allow for a further decrease in ventilation or, alternatively, if ventilation remains unchanged, more oxygen is available for the tissues not concerned with the mechanics of respiration.

In any condition in which the respiratory reserve is inadequate, tracheotomy should be considered as a therapeutic measure. The respiratory reserve can be assessed only if the patient is capable of cooperating sufficiently for his Maximum Breathing Capacity and Minute Ventilation to be estimated by spirometry. If the reserve is 2 : 1 or less, and adequate oxygen administration does not improve the reserve, tracheotomy is essential.

The more severely ill a patient suffering from respiratory failure is, the more one must consider tracheotomy, and the less one must consider the use of an artificial respirator as a first measure. If there is inadequate improvement after tracheotomy, the artificial respirator is applied to the tracheotomy tube. A cuffed rubber tube is more efficient than a metal one when used with a positive pressure respirator, but is more difficult to keep clean than is a metal tube. Either type allows suction of bronchial secretions, and prepares the patient for immediate artificial respiration. In selecting a tube, its suitability for connexion to the respirator must be ensured.

THE USE OF THE ARTIFICIAL RESPIRATOR

The use of the artificial respirator implies 'taking over' the patient's breathing so that a minimum amount of oxygen is wasted on the metabolism of the respiratory muscles. It helps the patient to meet his oxygen requirements and to eliminate carbon dioxide without the additional metabolic burden of his own hyperventilation. It entails the constant attendance of a nursing 'special' and the immediate availability of the physician. It should be employed before 'anoxia wrecks the machinery.'[14]

It is our impression that, with certain exceptions to be mentioned, artificial respiration is best performed by means of an intermittent positive pressure respirator through a tracheotomy tube. Pending tracheotomy, the respirator can be applied to an endotracheal tube or close-fitting face mask. Most of our experiences have been with the Radcliffe intermittent positive pressure respirator, but the following remarks refer to any respirator constructed on the same principles.

The pulse rate, blood pressure, respiratory rate, colour and temperature of the patient are, as usual, recorded. The respirator is adjusted to the same rate as the patient's spontaneous respirations and is set working at a low pressure (4 cm. H_2O) and small volume (300–400 ml. in the average adult). It is then attached to the patient and the effect observed. The primary aim is to ventilate the patient sufficiently to maintain a normal arterial oxygen saturation without administration of oxygen, without adversely affecting the pulse rate or blood pressure by too high a positive pressure, and without an abnormal drop or elevation of body temperature, measured rectally. The pressure at which the air is pumped into the patient, and its volume, are adjusted by small increments or decrements until this ideal is achieved.

If the positive pressure under which the air is introduced into the lungs is too high, it may compress the pulmonary capillaries in the alveoli of the lung, and decrease the amount of blood reaching the left ventricle. This may be detected clinically by an increased heart rate, a fall in blood pressure, or missing pulse beats due to recurring ventricular systoles that are too weak to reach the pulse on account of poor ventricular function. Such adverse effects are more likely to occur in a patient with atelectasis, and are less likely to occur in a patient with increased air-way resistance (e.g. bronchospasm), where the pressure is dissipated along the respiratory passages and is no longer high when it reaches the alveoli.

If, after varying the pressure and volume delivered by the respirator by small increments and decrements, the patient cannot be fully oxygenated as determined by his colour, without compromising the cardiovascular system, then an oxygen supplement must be provided by connecting the oxygen supply to the tap provided for the purpose, with a view to eliminating cyanosis. When this has been achieved, ventilation may be inadequate to prevent carbon dioxide retention, a condition that should be suspected if the patient's condition deteriorates. The diagnosis of carbon dioxide retention can usually, in these circumstances, be made clinically, but this is one of the occasions when the estimation of pH is necessary to substantiate the diagnosis of respiratory acidosis. If acidosis occurs, administration of alkali in the form of molar lactate is required.

Initially, high pressures may be needed for artificial ventilation but, as treatment proceeds, particularly if areas of collapsed lung become re-inflated, less force is required to stretch the lung.

Removal of secretions from the bronchial tree by suction through the tracheotomy diminishes areas of pulmonary collapse and decreases the air-way resistance. This is a distinct advantage of artificial respiration through a tracheotomy. A phase of hyperventilation with resultant excessive loss of carbon dioxide, heat and water may inadvertently be entered. The respirator must be adjusted so that the smallest pressure is applied to deliver sufficient air into the lungs to keep the patient well oxygenated without resorting to an oxygen supplement.

Any deterioration in pulse, blood pressure, colour, temperature or mental condition necessitates a search for the cause and should not be allowed to go unexplained and unremedied.

Our initial experience was with the tank respirator. It became apparent that major disadvantages apply to such respirators when used for the emergency of acute respiratory failure. The patient is almost inaccessible for nursing, observation and intravenous therapy. In the case of a very ill patient, movement from bed to the respirator may be dangerous. The very obese patient just does not fit the machine. There can be no certainty that the machine will be powerful enough to provide an adequate Minute Ventilation. The patient's ventilation must be constantly checked by spirometer or gasometer, and the temperature must also be carefully checked, watching for the dangerous conditions of hypopyrexia or hyperpyrexia. The tank respirator becomes relatively unworkable if tracheotomy has been performed, as the air-tight neck collar cannot be applied.

The machine should only be used on a patient who is not critically ill, and who will tolerate the procedures of trial and error that are necessary in finding the optimum ventilation.

The cuirasse respirator will not function if the patient does not relax and allow it to breathe for him. Patients have to be trained in its use. Its capacity is not as great as that of the 2 previously mentioned instruments. Patients without great resistance to air flow, e.g. cases of poliomyelitis or myasthenia gravis with respiratory failure, or a patient with chronic chest disease who is not critically ill and who can co-ordinate his breathing with the machine, are suitable for trial of this type of respirator. It may at least reduce the oxygen 'wastage' incurred by the muscles concerned with respiration.

THE TREATMENT OF HYPERPYREXIA

The use of fan and ice packs in treating hyperpyrexia may make the patient vaso-constrict and shiver. A safer and quicker technique has been an iced retention enema, as used for cases of heat stroke. If a drop of 4–6° F. is required, an average adult requires a 300 c.c. enema. Ice chips are added to cold tap water and the enema is administered just as the macroscopic ice disappears. The cooling effect is obvious within 5 minutes and is at its greatest within 20 to 30 minutes. The 4–6° F. temperature drop is far in excess of that which would be expected from a change in water temperature alone. It may serve to break a vicious circle in heat regulation. The microscopic ice that is still present requires latent heat for conversion to water. A possible contra-indication is air in the peritoneal cavity due, for example, to a perforated viscus, as rapid gaseous distension may occur. As the hyperpyrexial patient is disadvantageously affected by postural change, the enema should be administered with the least possible change in posture.

Following the initial cooling procedure, the optimum temperature should be maintained by making the room cool, and ensuring that a comfortable draught is present.

THE TREATMENT OF HYPOPYREXIA

Hypopyrexia (which requires a wide-range thermometer for its demonstration) in a patient who has undergone an operation, or in a

patient who is being artificially ventilated, has none of the advantages of artificial hibernation employed in a controlled manner for a short period of time. The general problem of hypothermia as a controlled therapeutic procedure is discussed by Evans and Gray.[15]

In uncontrolled hypopyrexia, the irreversible metabolic hazards likely to occur after a few hours are great.

An attempt should be made to regain a normal body temperature gradually, without jeopardizing the cardiac output to vital structures. The use of any measure that increases the temperature of the skin is contra-indicated, since the pooling of blood in the skin deflects blood from vital structures. The first step is to cover the patient with blankets. If this fails, it is tentatively recommended that the patient be given warm fluids intravenously or that the inspired air be warmed.

SUMMARY AND CONCLUSIONS

1. Suspect the possibility of respiratory failure in acutely ill patients with chronic chest disease, with 'stormy' post-operative states, and with neurological disturbances, such as head injuries, poliomyelitis or cerebral vascular accident, irrespective of the nature of the symptomatology.

2. The hazards of respiratory failure are increased by obesity, dehydration and hot humid conditions.

3. Clinical assessment of the course of a case under treatment in terms of pulse, respiration rate, blood pressure, colour and mental state is usually adequate. The measurement by spirometry of minute ventilation and of the maximum breathing capacity, and the calculation of respiratory reserve, are valuable additional methods of assessment in some cases and are essential in a few.

The estimation of arterial oxygen, carbon dioxide and pH may be essential in difficult cases.

4. In the treatment of acute respiratory failure, always try oxygen administration first. Administration of oxygen by nasal catheter is recommended. Determine whether this is adequate by the improvement or lack of improvement in the patient's condition, using the aforementioned criteria.

5. The patient's temperature must be observed rectally and should it rise unduly it must be reduced; should it fall unduly it must be raised to normal by the appropriate measures described.

6. Carbon dioxide narcosis is commonly erroneously diagnosed when patients with acute respiratory failure are being given oxygen. When present, it usually responds to correction of the method of oxygen administration.

7. Indications for tracheotomy are outlined and reasons are given for the axiom 'when in doubt, do a treacheotomy.'

8. If tracheotomy fails to improve the condition of the patient, the artificial respirator is added. The proper use of the artificial respirator entails constant observation of the patient's condition.

Our thanks are due to Dr. K. F. Mills, Medical Superintendent of the Johannesburg General Hospital, for permission to submit the case records for publication, and to the members of the medical, nursing and technical staff of the Johannesburg General Hospital for their co-operation in the management of some very difficult clinical problems.

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HAEMANGIOMATA

PATHOLOGY, HISTOGENESIS, TREATMENT

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The object of this paper is to crystallize modern views on this condition, and to suggest a common policy on treatment. The divergence of opinion on the treatment of this haemangiomata is considerable, even though the natural history of the condition has been well known since 1938.

The methods of treatment are almost legion. They vary from excision to carbon dioxide snow applications; the injection of sclerosing materials such as sodium morrhuate, sodium salicylate (or even the barbarous method of injecting boiling water). The radio-therapist will offer various types of radiation (beta ray radium irradiation, gamma ray treatment, radium implantation and X-ray administration and the latest P^{32} application). Some will advise immediate treatment, others will advise postponement for a variable period of time. Rapid growth may raise the fear of cancer in the minds of both the parents and the physician.

The natural history of this condition offers some considerable basis for correct prognosis and for intelligent conservative management. However, it requires a certain degree of courage on the part of the physician advising the parents to fly in the face of the advice of general surgeons, radio-therapists, etc.

Lister[12] reported on the results of managing 92 haemangiomata in 76 infants by observation only, withholding all forms of treatment. He found that by the fifth year a majority of them had shown regression. I personally have only occasionally seen any haemangioma persist in adult life. Those which will persist in adult life do not show any appreciable growth in early childhood.

INCIDENCE AND DISTRIBUTION

Lampe and Latourette,[7] in a 7-year survey at the University of Michigan Radiation Therapy Centre, state:

'There were 346 patients with cavernous haemangioma, 70 having more than one lesion, making a total number of 471 haemangiomata. In 394 observation extended over a sufficiently long time to gain insight into the cause of the disease when minimum active treatment was given. The cavernous and capillary haemangiomata are to be differentiated from the port wine mark and the spider naevus. Incidence figures for these lesions in childhood are not available, but it is essentially a common lesion.'

It is essential for the appreciation of this condition to have a thorough knowledge of the natural history of the course of the disease, which is entirely at variance with that of a neoplasm. It is present at birth or evidenced soon after. The lesion expands or grows sometimes very rapidly in extent and thickness. The growing phase of the lesion does not extend much beyond the age of one year and frequently ceases much earlier. After a variable static period, the haemangioma will slowly undergo spontaneous regression over a period of several years. The onset of regression can be identified by central blanching, decreasing thickness of the lesion and increasing looseness of the surface skin. Usually the lesion will be gone, or only traces will be apparent, by 5 years of age, while many involute completely before this age. Management of these lesions should be integrated with their natural history. The course early in life identifies those which will eventually regress. Those which do not exhibit any great change in childhood are the ones that may persist into adult life. Only minimum active treatment of any kind is required, often none is necessary and, above all, no form of treatment should be employed which may produce undesirable sequelae.

PATHOLOGY

There is no true tumour formation. The condition belongs to the type known as hamartoma, i.e. it is a malformation originating from a mass of vasoformative tissue, displaced or unused during embryonic development. Such tissue may produce lesions recognizable at birth or soon after, or not until later in life.

Most frequently the lesions are found in the skin, or skin and subcutaneous tissues, but they may occur in almost any tissue. The mass of vasoformative tissue consists of irregular spaces lined by primitive endothelial cells, masses of non-canalized tissue, more highly developed

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capillary structures, large vascular spaces, and quite mature arteries and veins. These may be found in varying combinations in any one case (Figs. 1, 2).

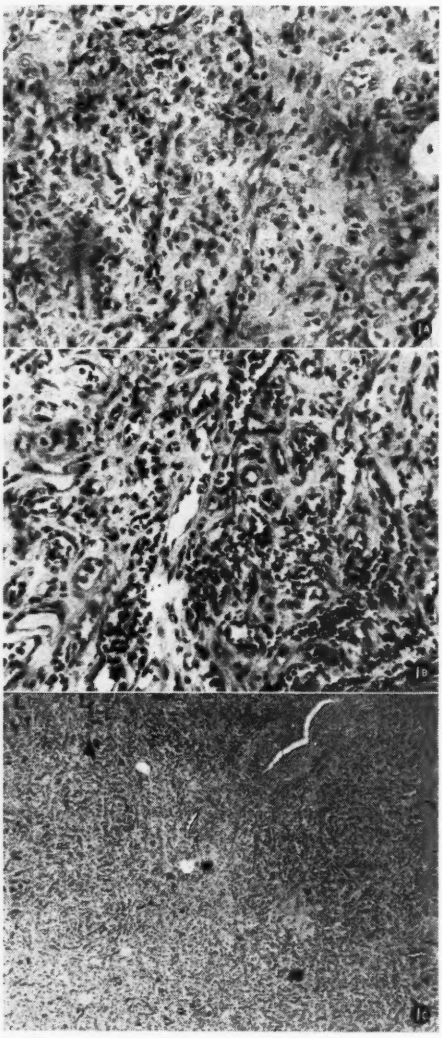

Fig. 1*a*. Showing masses of endothelial cells and and some primitive vascular channels.

Fig. 1*b*. Showing numerous primitive vascular channels lined with a single layer of endothelial cells. Stroma filled with fibroblasts and clumps of endothelial cells.

Fig. 1*c*. Showing some well-formed blood vessels and also primitive blood channels. A good deal of fibrous tissue is present, also masses of endothelial cells.

It is possible also to find that the preponderance of surrounding connective tissue may give it more of a fibrous element.

The spread of these tumours is not by increase of tumour cells, but rather due to canalization and establishment of a blood flow in fresh parts of an already existing malformation, or to changes caused by haemorrhage, inflammation or cystic degeneration. The extent of the lesion is, therefore, probably largely predetermined by the distribution and amount of vasoformative tissue unused or misplaced in the course of development of the vascular network.

The histological pattern which may be produced in this tissue appears to depend on how far the development and differentiation of these channels vary within the one hamartomatous mass. Mechanical factors, however, such as over-distention of the vascular channels, haemorrhage and fibrosis may contribute in some cases to the variable histological picture. In some cases the mass of poorly differentiated tissue may appear highly cellular and invasive.

Wallace[8] divides these conditions into 2 main groups, the *flat* and the *raised*.

The flat group consists of:

(*a*) *The spider naevus*, which is seldom present at birth and may often appear for the first time in adult life. It may undergo spontaneous regression in childhood, but seldom in adult life except when associated with liver disease or pregnancy.

(*b*) *The salmon patch*, pale pink in colour, it usually occurs in the nape of the neck, fading in a few months.

(*c*) *The port wine stain* or *naevus flammeus*. This has a deeper colour. A thin layer of capillary tissue in the dermis is permanent and a variation of this is a thicker, plum-coloured lesion, often associated with intracranial lesions, when it is known as the Sturge-Weber syndrome.

The raised type is subdivided into:

(*a*) *The superficial*, or better known as the *strawberry naevus*.

(*b*) *The raised* or *cavernous type*, which can extend into the deeper tissue for some considerable distance.

Combinations may occur of all the types outlined in this classification. A deep subcutaneous cavernous haemangioma may occur with an overlying spider naevus, so no classification is hard and fast (Fig. 3).

Innes[9] suggests that the cavernous haemangioma should be classified merely as superficial or deep. The value of such a simple classification is debatable.

DISTRIBUTION

This is indicated in Table 1.

TABLE 1

Site	*Percentage of Cases*
Head	50%
Face	34%
Trunk	32%
Extremities	18%
Forehead	8%
Eyelids and eyebrows	39%
Cheeks	20%
Nose	11%
Lips and chin	21%

69% are present at birth; 86% are either present at birth or develop within the first month; 14% develop only after the first month.

Relationship to Sex. One set of figures places it as 2.5 : 1 (female : male). The Oxford figures place it as 3 : 1 (female : male).

DESCRIPTION

The lesions are raised and red, of varying size and intensity of colour. They may be small or they may involve an entire limb, when it may lead to gigantism of that particular limb. The strawberry type is self-descriptive. The lesions empty on pressure as a rule, and there is no bruit. They may affect function in so far as they may be in the centre of the lip and interfere with feeding, or on the upper eyelid and interfere with the elevation of the lid and so interfere with vision. They may occur in the external auditory canal and so interfere with hearing. On the napkin area there may be repeated trauma from the napkin (Fig. 4). It may grow alarmingly in the first 6 months; after that it appears to grow with the child for another 6 months and then it begins to undergo regression and, even with the biggest lesion, all that may be left may be some redundant thickened skin, the removal of which does not present any great problem. It is due to

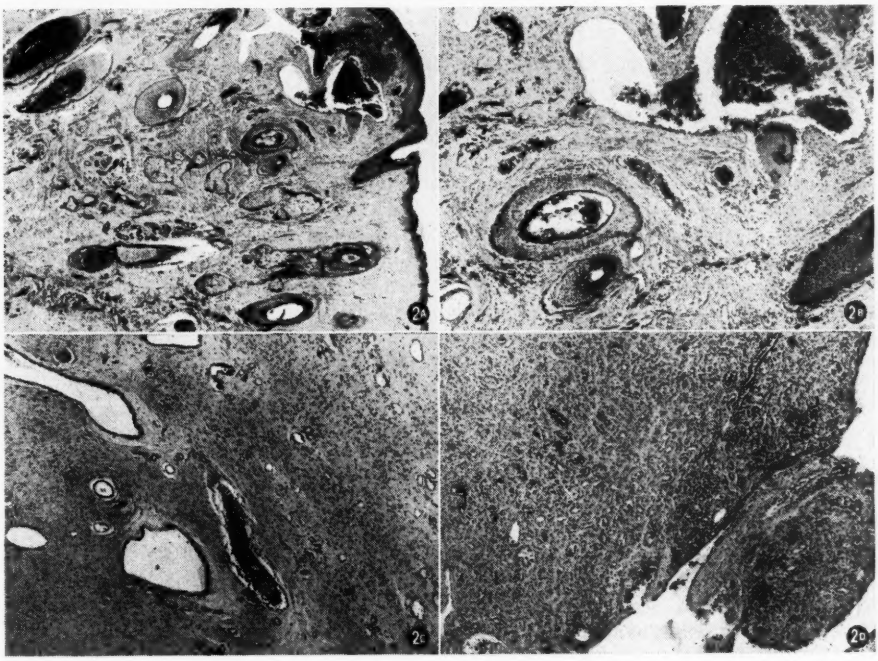

Fig. 2a. Photomicrograph of a lesion on the lip excised from a male adult. A small cavernous haemangioma with a focus of ulceration.

Fig. 2b. Higher magnification showing large dilated blood spaces lined with a single layer of endothelial cells and fibrous stroma.

Fig. 2c. Mixed capillary cavernous haemangioma showing numerous small capillary blood spaces; also occasional cavernous blood channels.

Fig. 2d. Capillary haemangioma showing very numerous capillary blood spaces, oedematous stroma and also some clumps of endothelial cells.

the phase of increase in size, which at times may be alarming, that the fear of malignancy arises. Then drastic therapeutic measures (such as radiation, injections and surgical or other means) may be undertaken, resulting in undesirable scarring, radiation damage of soft tissue, decreased bone growth. It may even be reported as showing a highly invasive tissue, possibly malignant.

skin gradually decreases in thickness and considerable regression may occur before the area of the lesion decreases. The progress of involution extends over a period of years and, in the most cases, by the age of 5 years the lesion is entirely gone or only traces remain. This is true without active treatment. In bulky lesions, additional time may be required for adjustment of redundant skin.

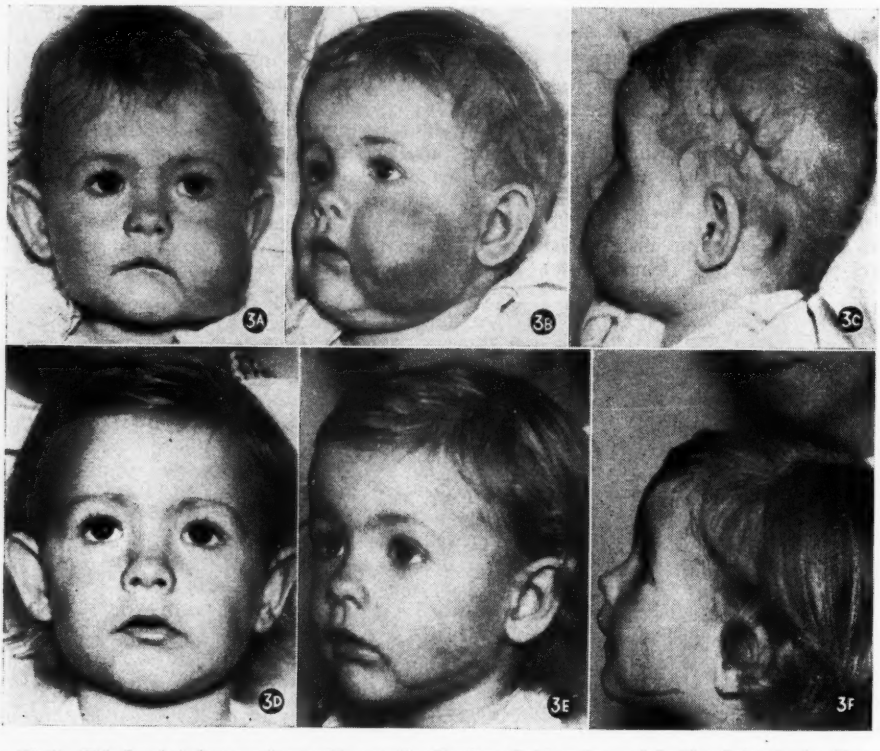

Fig. 3. This female infant was born with a small collection of skin veins on left side of the cheek. Two months later it became like a bruise and began to swell. It grew rapidly for 4 months, was then stationary for some months. Thereafter it suddenly grew much bigger. It seems to fluctuate in size at times, becoming tense and hard. Operation: The tumour shelled out from the deep tissue of the cheek, with the result illustrated. Result as in photographs. Biopsy Report: Cavernous haemangioma undergoing sclerosis.

After the maximum size is attained, a stationary period of some months may ensue before signs of regression appear. The first sign of regression will be a change from the original colour to a less red colour and then to a greyish hue. The changes occur in the centre and spread to the periphery. There is a decrease in tenseness of overlying skin, manifested by a slightly wrinkled appearance. The

TREATMENT

Various types of treatment have been employed to date. These illustrate the state of hopeless confusion in the general outlook towards this condition.

The data from America, Oxford and Glasgow, illustrate the results of conservative treatment.

The first of a group of methods aims at sclerosis, thus failing completely to realize that fibrosis or sclerosis is the ultimate end result of the natural history of the condition. No better sclerosis can be obtained than by leaving the condition to follow its natural course. The commonest methods of achieving sclerosis are:

(*a*) By heat.
(*b*) By cold (carbon dioxide snow).
(*c*) By irradiation, surface radium, beta radiation, radioactive P^{32}, X-rays, radiation in the form of plaques and radium needles.
(*d*) By the injection of sclerosing fluids, such as boiling water, saturated saline 33%, etc.

In a vast percentage of cases this treatment is not necessary, and it can lead to disastrous results in the form of severe scarring, radio-dermatitis or even radionecrosis; interference with bone growth, chronic infection. With the injections of sclerosing fluids, some disastrous results in the way of massive sloughing can occur, apart from the pain and discomfort inflicted.

None of these methods should be employed, especially CO_2 snow, without first allowing the natural history of the condition to take its course. There can be no object in applying any of these methods in a condition which in over 80% will require no treatment whatsoever.

SURGERY

No surgery should be contemplated on these children except where function is being interfered with, e.g. cases of the upper lid, which lead to inability to open the eye or, in the external auditory meatus, when there is interference with the development of hearing. In the centre of either lip it may be large enough to interfere with feeding, and on the buttock it may cause considerable difficulty due to injury from the napkin. Otherwise no surgery should be contemplated until the lesion has been given every chance of undergoing the natural regression which occurs in the vast majority of these cases. When the child is over 5 years, it is able to withstand surgical procedures much

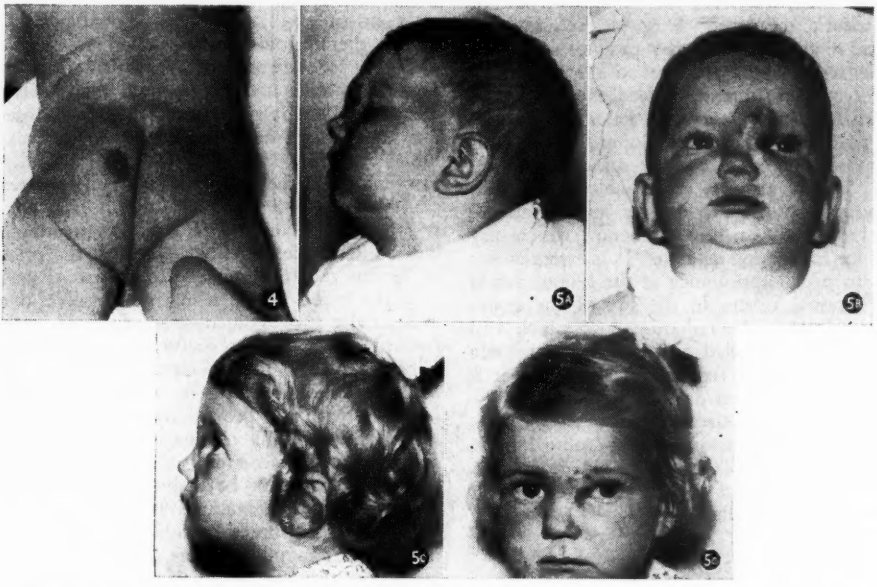

Fig. 4. Male infant aged 3 months. Birthmark (capillary haemangioma) noticed at birth. It is growing and has ulcerated in the centre. Conservative treatment is indicated unless the napkin causes repeated trauma, ulceration and sepsis.

Fig. 5. At birth the mother noticed a small pale pink spot in the glabellar region, the size of a 3d. piece. It was treated by a radium plaque at the age of one month, at 3 months and at 6 months. The lesion grew bigger in spite of treatment. The patient was then advised to have surgery. The large swelling illustrated is partly due to an overlying radio-dermatitis. No treatment whatsoever was advised, with the result shown in Fig. 4*c* and 4*d* taken 2 years later. The haemangioma has regressed almost entirely, but the radio-dermatitis has left her with a large, unsightly skin blemish, which is also potentially dangerous. This will require excision when she is a little older and some form of plastic repair will be required.

more easily than infants can and if, by 5–7 years there is no evidence of regression and there are the general indications for removal, it could then be done.

Very often the parents force the doctor into a decision to operate, but every attempt should be made to resist this pressure unless there are very definite indications for surgical interference. In one case a child had a large subcutaneous haemangioma on the left cheek and, due to pressure by the paediatrician and the parents, I was forced to undertake a hazardous operation to remove this tumour, running the risk of damage to the facial nerves and leaving the child with a severe scar. Fortunately the result was extremely satisfactory (Fig. 3), but the pathological report indicated that this lesion was undergoing sclerosis and spontaneous regression, and if to operate had been resisted, the tumour would have subsided without any surgical interference whatsoever and consequently without any hazards.

The chief hazard in the management of this condition in infancy does not arise from the disease itself, but from the enthusiastic use of therapeutic measures. Surgical excisions and plastic re-arrangements may produce some cosmetic results very inferior to the results of conservative treatment. Indeed, there is always the risk of unpleasant scars, keloid formations and possible carcinoma development; also limitation of bone growth with resulting deformity (Fig. 5). It is quite unjustifiable to apply to a benign condition, which by its very nature mostly regresses, a form of therapy which may produce hazards of its own. It is essential not only to get disappearance of the lesion, but to have normal tissues in the site of the lesion decades later. The radiation dose which will avoid all late sequelae, particularly when given in multiple small repeated quantities over a period, has not been precisely established.

Lampe and Latourette[7] suggest 300 r as a single dose at one sitting for most lesions. For larger lesions 500 to 600 r given over 5–6 days. The object of this treatment is to limit growth. The results:

1. No change.
2. Mild blanching.
3. Considerable regression of colour and bulk which is maintained or may, after a short period, enlarge again to almost the original size. This will not occur if the lesion has passed beyond its growth phase.

It is of interest to note that when a lesion has ceased growing, incomplete excision may be carried out without fear of recurrence.

Many radio-therapists employ empiric dosage. One or two doses of X-rays are given; then they wait for eventual resolution. Despite this, many will not agree that spontaneous involution does take place and believe that all such lesions require treatment. However, the realization that spontaneous involution takes place has been recognized and demonstrated by an increasing number of X-ray workers, as exemplified by publications of Walters[13] and Rouchese.[14]

Walters[13] reports 83 untreated cases which involuted. With all this evidence I feel that, except in very exceptional cases, radiation has no place in the treatment of this clinical entity.

CONSERVATIVE MANAGEMENT

The first step is to identify the type of lesion and to exclude all except the cavernous and strawberry types. The next most important step is to separate those which will involute spontaneously from those which will not. This is governed by the growth pattern exhibited by the lesion early in the infant's life. Those lesions which enlarge during the first 6 months and cease growing after the age of one year, will involute. Lesions which do not grow early in life will not regress spontaneously, though there are exceptions.

There are haemangiomata which may be present at birth and not exhibit enlargement during the first few months of life, but subsequently, perhaps after the first 1–2 years, exhibit growth which may continue steadily. Histologically they contain partially formed adult vessels with smooth muscle. This type is rare. It is doubtful if radiation treatment will obliterate these lesions except at the price of serious radiation damage to normal tissues.

If the lesion is one which will resolve, one must advise strongly against any form of interference whatsoever. Careful clinical records, photography and measurements must be made and the child observed at regular 6-monthly intervals, with the proviso that if the parents notice any alarming change, then they are to communicate immediately.

The parents must be taken fully into one's confidence and the natural history explained to them. They should be told that there is no need for panic and that they should accept the temporary disfigurement. If one's advice can be backed up with photographic records of other cases, it will be easier to assuage their fears and anxiety. Above all, they should be reassured that there is no danger of malignancy. Exceptions have to be made if there is any interference with function at any time. In most cases, at the next visit, the mother will come full of smiles, ready to report herself that the lesion is smaller and less dark. If the

regression continues, there is no need for any further treatment, except possibly later to excise any redundant thickened skin when the child is a good deal older. This would be a very minor procedure.

Wallace[8] says:

'When the lesion is in a conspicuous area, it may be necessary to try and hasten involution in order to relieve parental distress. For this the choice is between very small doses of X-ray or radium or sclerosing solutions.'

Here it is a choice between two evils. The possibility of damaging growing germ centres in providing an effective determined dosage of radium and the psychological upset of repeated treatments and the hazards of anaesthesia, must be borne in mind. *Moreover, it has not yet been proved that either of these methods may not interfere with involution.*

Wallace goes on to say:

'The rapid growth in early infancy is seldom an indication for drastic surgical interference . . . There can seldom, if ever, be any justification for the gross and mutilating surgery which is occasionally practised . . . Most recorded reports of malignant changes in these haemangiomata bear the imprint of panic, combined with an inadequate knowledge of their natural history.'

He draws attention to the extremely rare strawberry type which does not enlarge in size out of proportion to the growth of the child, in which malignancy has been recorded at or after puberty but never before. Therefore it is easy to recognize these lesions at the age of 6 or 7. Excision would then be indicated.

He states:

'When the haemangioma involves a mucous surface, such as a lip, it seems to involute less frequently and to be less complete than elsewhere. The presence of veins arranged in a stellate formation around the lesion seems to be associated with a worse prognosis.' (Fig. 6).

A small single dose of X-rays for selected cases is recommended by some, but the present writer cannot agree to this.

The following data illustrate the result of conservative treatment:

Wallace[8] divided his cases into 4 groups:

Group 1: It is impossible to detect the site of the lesion.

Group 2: The patient is left with a slightly atrophic skin which causes no disability, cosmetic or otherwise.

Group 3: Involution is partially complete, but some slight infiltration is left, usually with atrophic skin. No treatment is usually required for the residual defect but, if necessary, simple surgery suffices.

Group 4: There is no involution.

He had 208 cases of strawberry haemangiomata only, with no evidence of a cavernous element, comprising a total of 290 lesions.

Group 1:	120
Group 2:	157
Group 3:	10
Group 4:	3

There were 98 patients with 121 cavernous lesions:

Group 1:	15
Group 2:	78
Group 3:	20
Group 4:	8

The Oxford figures for the years 1944–1948 were:

Total Number of Cases: 81.

Methods of Treatment:

Conservative:	25
Conservative plus surgery:	2
Surgery alone:	34
Diathermy:	2
Radiotherapy:	9
Injection therapy:	1
	73
The results were:	
Incomplete records:	8
	81
Cases under conservative treatment not followed up:	6
	75
Port wine stains:	7
	68
Conservative treatment not tried:	13
	55

The successful conservative results were therefore reduced in the vicinity of 70%. In a subsequent communication from the Oxford Department, the results since then show an 80% recession under conservative treatment.

TABLE 2: RESULTS IN HAEMANGIOMA

	Untreated	*Cauterization*	*Irradiation*	*Surgery*
Number of lesions	60	68	62	136
Satisfactory result	77%	35%	24%	22%
Moderately satisfactory result	20%	50%	40%	41%
Unsightly result	2%	15%	25%	37%

Lampe and Latourette,[11] dealing with spontaneous recession *versus* treatment, state: 'The phenomenon of spontaneous regression in these lesions has slowly gained recognition.' Table 2 illustrates their experience.

They stress the importance of correct identification of type to separate the involuting from the non-involuting type. They state:

'Lesions which enlarge during the first few months of life and cease growing before one year will involute. Lesions which do not grow early in life as a rule do not regress spontaneously . . . The principal danger in management of the involuting

variety arises not from any feature of the disease, but from over zealous therapeutic measures . . . The indications for radiation are few and apply infrequently.'

They confirm the importance of sound parent counselling with accurate photography and regular observation. They state:

'Haemorrhage rarely occurs from these haemangiomas . . . (and) Bleeding that has occurred has been readily controlled by compression bandage . . . Conservatism more essential in the large advanced lesions.'

There is a type of haemangioma which is considered a possible malignant condition, but is extremely rare. It is known as a multiple malignant metatasizing haemangioma. This clinical condition is, in my opinion, the type where the skin manifestations do not show growth in early infancy.

There is a recorded instance of fibrosarcoma occurring in these conditions but here, again, all the malignancies occur after puberty, so that the dictum is that if the lesion has not regressed spontaneously by the age of 5 or 6, surgery could be resorted to at that date.

Variation of opinion is indicated by the following passages:

Pfahler[1] advises radiation for the majority within the first few months. Larger lesions should be treated by irradiation before caustics have been used or ulceration has occurred. Sometimes treatment is best supplemented by electrosurgery or scalpel surgery. He does not say whether his opinion is confined to cavernous lesions and he loses sight of the natural history of the condition.

Bean[2] quotes the condition of dyschondroplasia and haemangioma. He reported on 3 cases where the conditions occurred together in the last 2 years and he reviews 7 additional cases reported since 1942. It may be suspected early in life when the unusual haemangioma does not regress or disappear. He states:

'The multiple effects of a single gene are responsible . . . the patient with one or other of these clinical states should be examined for disorder of the other apparently unaffected tissue.'

Myers and James,[3] in discussing the comprehensive management of cavernous haemangioma of the lower extremity, advocate stripping of the veins and claim good results.

Figi[4] states that these conditions lie in an ill-defined zone between new growths and congenital abnormalities and they are almost invariably benign in their clinical behaviour. Accordingly, it is important that nothing be done therapeutically that might produce complications of a graver nature than the original lesion. When feasible, surgical excision of both cavernous and capillary haemangioma is being resorted to more and more, as it is safer and produces fewer complications than the other methods of treatment and gives satisfactory cosmetic results. When irradiation is used, extreme care must be taken in evaluating the dosage. Cavernous haemangiomata, whose situation render excision inadvisable, can best be treated by injection of sclerosing solution or electrocoagulation, or a combination of these methods.

In discussing the question of spontaneous regression he quotes numerous authorities where this has occurred in up to 95%. Yet he states:

'Unfortunately this spontaneous regression is not always the case and spontaneous regression of port wine stains and cavernous varieties is not observed.'

Whilst agreeing about the former, I cannot agree about the latter type. He will only concede the strawberry type as liable to undergo regression and yet it and the cavernous type are essentially identical lesions.

He goes on to indicate some agreement on the natural history and it would seem that his indications for operation are largely functional as indicated here. He stresses the danger of haemorrhage which, it is submitted, is grossly over exaggerated.

Johnson and Dockerty,[5] in discussing haemangiomata of the extremities, say that reliable laboratory data have been presented to link the etiology of these tumours to the carcinogenic hydrocarbons. Classified as discrete and diffuse, all diffuse show invasive properties; only 23% are discrete. All were treated by surgery without fatality.

McComber[6] says on the surgical aspects of haemangiomata, that if there is any intervention, it must be surgical. Indications for surgery:

1. A tumour so large that it cannot be destroyed or removed by physical agents.
2. The tumour is growing faster than the individual, especially when it bulges on crying or straining.
3. Ulceration on haemorrhage.
4. When patients prefer a scar or a graft to a birth mark.
5. When treatment has failed or left disfiguring or potentially dangerous tissue changes.

I consider that none of these is a justifiable indication.

Matthews[10] is in favour of interference at an early date. He does, however, recognize that birth marks are commoner in children than in adults. It necessarily follows that some regress spontaneously and disappear without treatment, but he says that 'some clinicians believe that none should be treated in child-

hood, even if they are growing, in the hope that regression will occur later.'

This policy is open to severe criticism. A certain number of tragedies will occur from rapid extension of the lesion which may become inoperable, ulcerate or even kill the child. The mental suffering of a child and the parents is unnecessarily allowed to continue. It is often acute in facial lesions, particularly in a child during schooldays. He completely misses the whole essential point, that the vast majority clear up by school days. If it does not regress, this should be removed before the child goes to school.

I have seldom seen one of these simple cavernous and strawberry haemangiomata persist into schooldays. He pays scant attention to natural history and is, therefore, in no position to formulate a fixed policy.

His indications for treatment are as follows:

1. *Growth.* He talks of new cells budded off from the vasoformative tissue. This statement can be challenged, as has been indicated previously. He admits that there is some canalization and vascularization of pre-existing vasoformative tissue, but insists that some new growth occurs at the same time.

2. *Cosmetic Blemishes.* He says: 'The advisability of treating birth marks, which are not extending or are growing no more rapidly than the individual, is obviously controversial.' He is obviously confusing the types and is referring to port wine stains which, it is accepted, do not regress.

Under *Cosmetic Blemishes* he says:

'In young children the responsibility for a decision rests on the doctor. He should be guided by knowledge of the usual behaviour of that particular type of birth mark, its situation, its proximity to structures which would be dangerous or render treatment difficult, and by the psychological state of the child and the parents.' The parents' state should not be an indication for treatment. He does say that each case must be assessed individually by weighing up all the factors.

3. *Haemorrhage.* He describes this occurrence as a surgical emergency calling for immediate treatment, but overstresses its importance or frequency. If bleeding is severe and repeated, it may require surgery.

4. *Ulceration.* He considers this a strong indication. If there is chronic ulceration and sepsis, and if the lesion is in an awkward place, e.g. the napkin area, this will not be controverted. He makes the bald statement that 'in my experience, regression of cavernous haemangioma is not to be expected.' He does not consider it justifiable to postpone treatment in a strawberry haemangioma in the hope that spontaneous regression will occur.

He discusses diffuse haemangiomatous gigantism where the whole limb is riddled with capillary haemangiomatous tissue. Excessive oxygenation causes overgrowth of all structures of the limb which quickly becomes longer and stouter than its fellow. After only a few years this causes a pressure on the right side of the heart, which fails, and kills the child. Early high ligation of the main artery supplying the limb is the only way to save the child's life. Procrastination until the heart is dilated is fatal. Even amputation does not save such a case at this late stage.

CONCLUSION

An accurate knowledge of the natural course of this condition and its pathology is essential. It is not a neoplasm.

Its growth is not by increase in tumour cells.

It goes through a natural course; 80% of the cases undergo regression.

In early infancy, the only indications for operation are serious interference with function.

There is plenty of time to wait and see if the cases undergo regression. If they do not, they can be removed at a time when the child is better able to be subjected to surgery.

Those cases which will persist into adult life and possibly give further trouble, can readily be recognized and dealt with before puberty.

Above all, no treatment which is going to leave unpleasant sequelae in the form of scars, unstable skin or loss of tissue or deformity, should be undertaken in a condition which is so essentially benign and which runs such a sterotyped course in most cases. To subject an infant to any of these hazards is totally unjustifiable.

No surgery should be contemplated on these children except where function is being interfered with, e.g. cases on the upper lid which cause inability to open the eye; in the external auditory canal, where there is interference with the development of hearing; in the centre of either lip, where it may be large enough to interfere with feeding; and also on the napkin area, where it may cause considerable difficulty as a result of injury from the napkin. Otherwise no surgery should be contemplated until the lesions have been given every chance to undergo the natural regression which occurs in the vast majority of these cases.

When the child is over 5, it is able to withstand surgical procedures much more easily than infants can, and if by the age of 5 or 7 there is no evidence of regression and there are the general indications for removal, it could be done then.

It is hoped that this review will serve as a guide for general practitioners and others seeing this type of case, so that the correct advice may be given to the anxious parents.

I wish to thank Prof. T. Pompfret Kilner, *C.B.E.*, F.R.C.S., Emeritus Professor of Plastic Surgery, Oxford, for placing records and photographs from his Department at Oxford at my disposal and for permission to publish them;

Dr. J. A. Wainwright, Senior Lecturer in Pathology, Medical School, University of Natal, for arranging for photomicrographs;

Mr. Stewart, Head of the Photographic Section, Department of Pathology, Medical School, University of Natal.

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APPENDIX OF ILLUSTRATIVE CASES

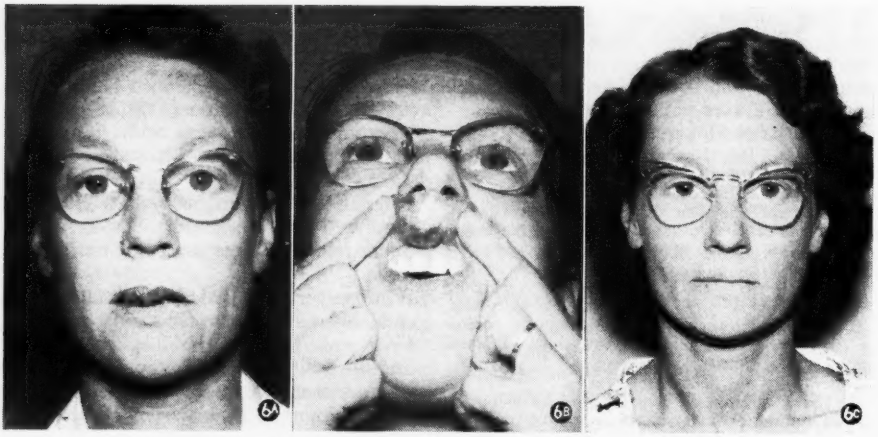


Fig. 6. Female, aged 32 years with a subcutaneous cavernous haemangioma in the substance of the upper lip. This was enucleated and the lip resutured after readjustment of the mucosa. Biopsy confirmed the diagnosis. This is one of the few situations where recession is not common.

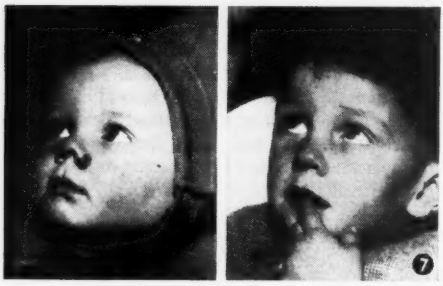


Fig. 7. Male infant 1 year old. *Left:* Born with a red spot on the left nostril margin which increased in size until age 6 months. No increase since. Capillary cavernous haemangioma. *Right:* At age $5\frac{3}{4}$ years. No treatment. No lesion remaining.

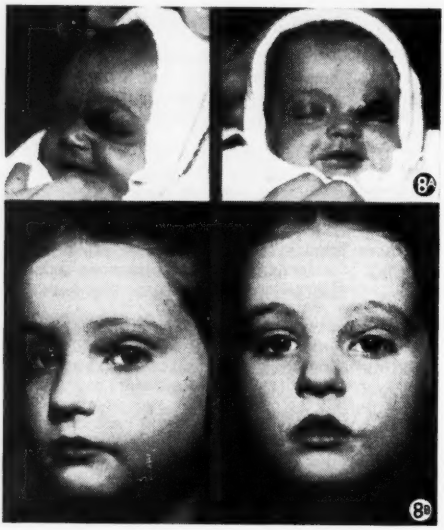


Fig. 8. Female infant aged 2 months. *Fig.* 8*a* shows a large naevoid projection on the left upper eyelid. Mixed caverno-capillary haemangioma with a considerable deep portion. Eye opens only partially. *Fig.* 8*b*. 6 years later. No treatment. Haemangioma has disappeared. There is some redundant skin which may take up in time.

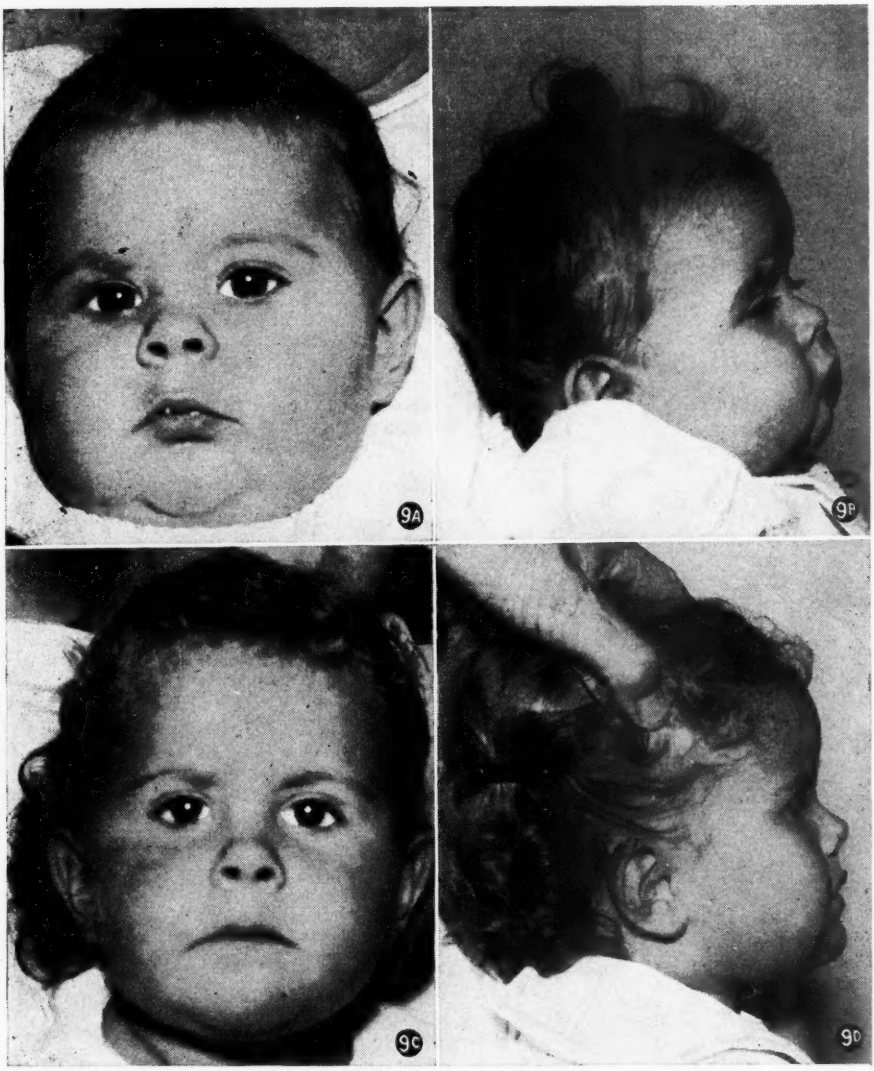
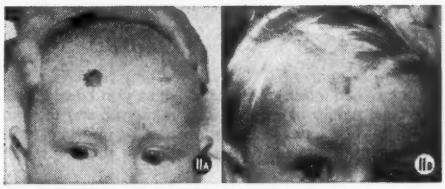


Fig. 9. Female infant aged 5 months. The mother noticed a small lump the size of a split pea on the right eyebrow at birth. It has been increasing in size during last 2 months. She has other birthmarks on the body, viz. scalp, right cheek, left lower abdomen, back. The mother had a birthmark on the neck, but it disappeared on its own. The father has a birthmark on the right shoulder. The eyebrow lesion has not been treated. She has been seen regularly, and it is gradually disappearing. At the last visit (22 months after the first) it was found to be completely flat and scarcely visible.

Fig. 11. Male infant. Strawberry naevus. The mother noticed a small pinkish patch on the right forehead. At 6 weeks it started getting darker and bigger until it reached the size first seen at the age of 2 years. Nine months later it was less prominent, flatter and with a pale spot in it and not so dark.



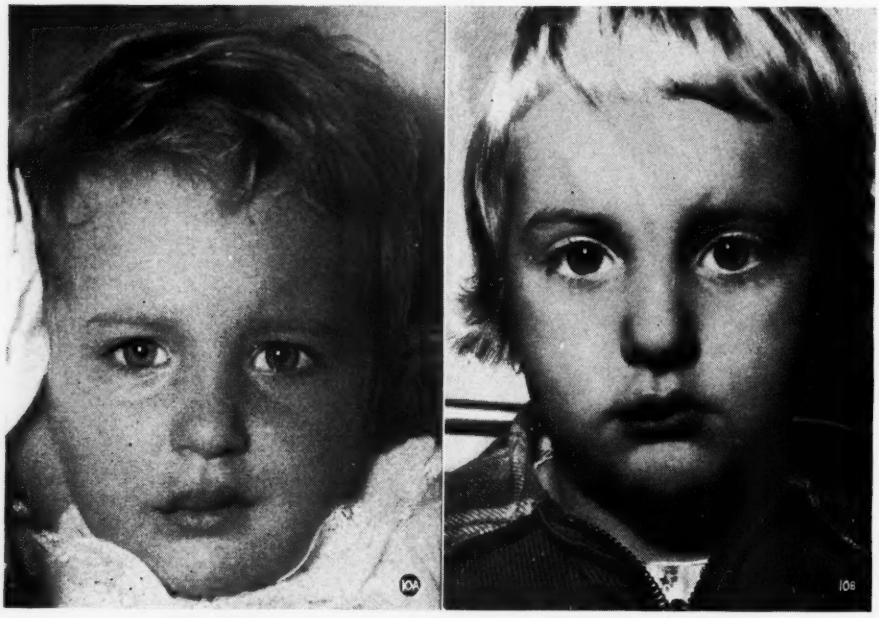


Fig. 10. Female infant aged 2 years. At birth the mother noticed a swelling of the upper lip. It looked as if it had been bruised. It did not interfere with feeding and did not bruise. The mother says the external blue marks have become less, but the swelling of the lip only increased with her growth. Excised: Lesion consistent with haemangioma. One reason for the removal was to avoid possible further distortion of skin vermillion junction line in a female child. Later this thickening of vermillion will be dealt with if necessary.

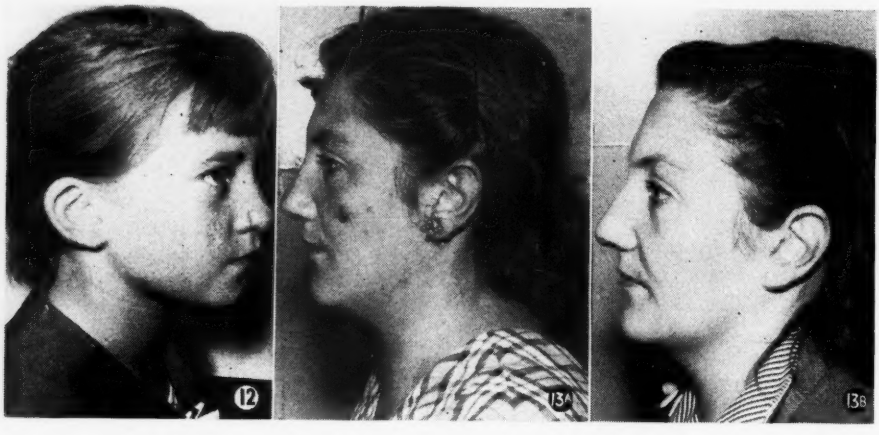


Fig. 12. Female aged 10 years. She was born with a strawberry-coloured birthmark on the right cheek. It grew bigger during the first 6 months of life. Treated at age of 8-9 months by means of 4 applications of radium. A depressed, pale, papery scar with telangiectases; very obvious radio-dermatitis which will require excision with all attendant difficulties of closure.

Fig. 13. Female aged 27 years. Nothing showed on the face until 3 weeks before when a white spot developed. She pricked it with a needle; it bled a good deal, developed a scab, bled on washing and increased in size and became redder in colour. It was excised and the wound closed by direct suture. Biopsy: Skin showing a polypoid capillary haemangioma. The unusual feature is the sudden appearance at the age of 27 years and following a pinprick. It is doubtful if this is a true haemangioma.

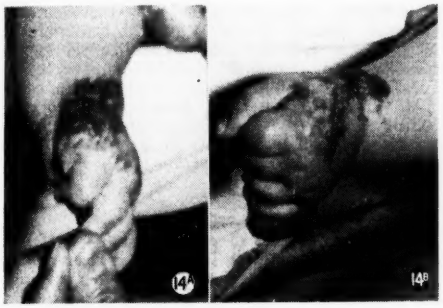


Fig. 14. Female infant aged 4 months. Mixed cavernous and capillary haemangioma. Two weeks after birth the mother noticed marks on the left hand and wrist. They have become darker since then. The mother does not think they have got bigger except with growth of hand. Management was conservative. She was seen at intervals and showed gradual retrogression. At the last visit ($2\frac{1}{2}$ years after the first visit) it was noted that it had regressed considerably in colour and extent. (Original measurements: $2\frac{1}{2}$ x $1\frac{1}{2}$ inches; Now: $1\frac{1}{2}$ x $\frac{1}{2}$ inches).

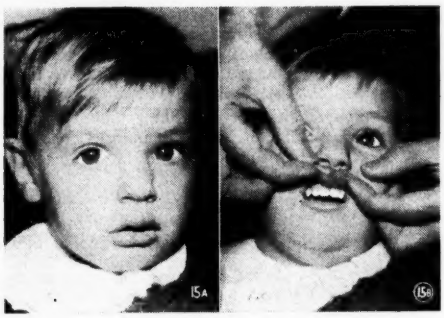


Fig. 15. Male infant aged 1 year 10 months. Born with a blue swelling on the middle of the red margin of the lip. It has grown to the present size. It stopped growing for past 10 months and is not interfering with him in any way. Management conservative.

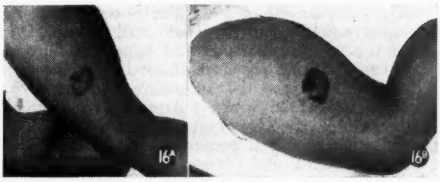


Fig. 16. Female infant aged 15 months. Strawberry naevus. The mother noticed a small birthmark on the left thigh when the child was born. It grew quite considerably. Latterly it has grown with child. It has always had pale patches in it. It was more raised than at the time of examination. Ten months later: the lesion was flatter and the pale areas more numerous. The mother is convinced it is receding. No treatment.

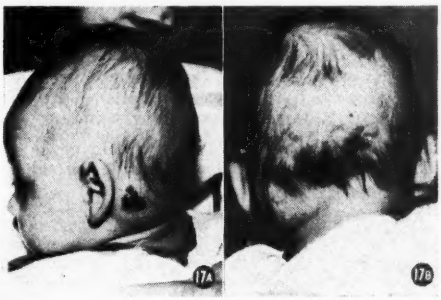


Fig. 17. Female infant. Cavernous haemangioma. She was seen at 5 months. A small spot was noticed 3 weeks after birth. Since then it has grown bigger and more prominent and darker. Treatment conservative.

NOTES AND NEWS : BERIGTE

Mr. H. Kramer has commenced practice as an Obstetrician and Gynaecologist at 902 Medical Arts Building, Jeppe Street, Johannesburg.

Telephones: 23-1888/9.

In the past 10 years Mr. Kramer has been doing post-graduate work in the United Kingdom at centres in London, Liverpool, Manchester and Edinburgh, as well as in the United States of America.

* * *

THE ASSOCIATION OF SURGEONS: PRETORIA GROUP

The next meeting will be held on Friday, 23 September at 5 p.m. in the Upper Lecture Theatre, Clinical Buildings.

Dr. C. A. R. Schulenburg will report on the *Durban Surgical Congress.*

All practitioners are welcome.

Mr. Paul Marchand, M.D., Ch.M., F.R.C.S., of Johannesburg has returned from the United States of America and has resumed practice. He held a Wellcome Travelling Fellowship and undertook study in open-heart and other cardio-vascular surgery in the United States of America.

* * *

SOUTH AFRICAN MEDICAL & DENTAL COUNCIL

The 72nd ordinary meeting of this Council will be held in the Committee Room (Room No. 95), First Floor, Public Library, Johannesburg, commencing on 12 September 1960 at 10 a.m.

* * *

ASTRA INTERNATIONAL (SWEDEN)

Westdene Products (Pty) Ltd. announce their appointment as sole South African agents for Astra International of Sweden.

Astra was founded in 1913 and since then it has developed steadily year by year until to-day it is one of the largest pharmaceutical houses in Europe. More than 2,200 people are employed in its Swedish factories and in the 14 subsidiary companies in various parts of the world. Almost 250 of these employees are actively engaged in research projects covering pharmaceutical preparations, surgical instruments, agricultural and chemical industrial products, etc. Astra's present manufacturing programme covers no less than 400 different products.

The best known of the many products which have been discovered in the Astra Research Laboratories is, of course, Xylocaine—the original lignocaine which is still regarded by many as the finest local anaesthetic available. However, many more products of original research from the Astra Laboratories will be reaching South Africa during the coming months as a result of the new association with Westdene's Ethical Division. Details regarding these products will be announced as soon as they become available.

The Monthly General Meeting of the Southern Transvaal Branch of the Medical Association of South Africa will be held at Medical House, 5 Esselen Street, Hospital Hill, Johannesburg, on Tuesday, 20 September 1960, at 8.15 p.m.

Mr. F. W. Holdsworth, President-Elect of the British Orthopaedic Association and one of the leading orthopaedic surgeons in Britain, will talk on: *The Etiology and Prevention of Deformities in Poliomyelitis.*

* ° *

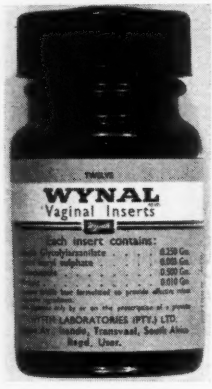
Dr. A. Zoutendyk, Head of the Blood Transfusion Service and Department of Immune-Haematology will officially represent the South African Institute of Medical Research at the Eighth Congress of the International Society of Blood Transfusion in Tokyo during September. He will read a paper on *Rh Factors C and G in the South African Bantu.*

He will also attend the Eighth International Congress of Haematology which is being held in Tokyo in September.

PREPARATIONS AND APPLIANCES

WYNAL VAGINAL INSERTS

Wyeth Laboratories (Pty.) Ltd., announce the introduction of a new product for the complete treatment of vaginal infections.



Wynal vaginal inserts are highly effective in the treatment of vaginitis caused by trichomonas, monilia, bacterial infection or vaginitis of mixed etiology.

Wynal inserts contain:

Bismuth glycolylarsanilate, for its trichomonicidal action and effectiveness against fungi and bacteria;

Sulphathiazole, for its action against bacterial infection;

Sodium lauryl sulphate, for detergent action to facilitate dispersal of the compound and permeance of the infecting matter; also

Allantoin, for its healing properties.

Formula: Each insert contains:

Bismuth glycolylarsanilate	250 mg.
Sulphathiazole	500 mg.
Allantoin	10 mg.
Sodium lauryl sulphate	3 mg.
Lactose, dextrose, sucrose, magnesium stearate and corn-starch ...	*q.s.*

in a hydrosoluble base which facilitates efficient liberation of the active ingredients.

Directions: One *Wynal* insert should be placed high in the vagina every other night for 10 to 14 days.

Supplied: Bottles of 12.

CARVASIN

A NEW CORONARY VASODILATOR

Wyeth Laboratories (Pty.) Ltd., announce the introduction of a new long-acting coronary vasodilator.

Composition: Each *Carvasin* tablet contains isosorbide dinitrate, 10 mg. (1,4,3,6-dian-hydrosorbitol-2,5-dinitrate).

Action and Indications: *Carvasin* is a long-acting coronary vasodilator of unprecedented effectiveness, indicated for the treatment of angina pectoris.

Carvasin offers the following clinical benefits:

(*a*) *Rapid Onset of Action.* Patients usually experience benefits within 15 to 30 minutes—about half the time encountered with pentaerythritol tetranitrate.

(*b*) *Prolonged Action.* A single dose produces effects which persist for 4 to 5 hours. Convenient *q.i.d.* dosage, therefore, is highly satisfactory for most patients.

(*c*) *Greater Effectiveness. Carvasin* significantly reduces the number, duration and severity of anginal attacks, and has done this in a manner demonstratively superior to that of pentaerythritol tetranitrate. It should be noted in this connection that the average milligram dosage for *Carvasin* is approximately half that for PETN.

(*d*) *Greater Safety.* The only side effect observed to date has been headache, which usually responds to acetylsalicylic acid and abates as therapy continues. Persistent headaches can usually be controlled by reduction in dosage. It should be noted that headache is normally considered an indication of effective pharmacodynamic activity.

Carvasin's toxicity is extremely low: approximately 40 times the therapeutic dose is required to produce symptoms of toxicity.

Administration and Dosage: The average dose of *Carvasin* is 1 tablet (10 mg.) 4 times a day, half an hour before meals and at bed-time. For optimum effect, individualization of dosage is necessary. The dosage range is 5 mg. to 20 mg.

Contraindications: Like all nitrates, *Carvasin* should be given with caution to patients with glaucoma.

Supplied: Bottles of 50 tablets, 10 mg. per tablet.

REVIEWS OF BOOKS

DISORDERS OF CONNECTIVE TISSUE

Heritable Disorders of Connective Tissue. By Victor A. McKusick, M.D. (1960. Pp. 333, fully illustrated. £5 2s.). St. Louis: The C. V. Mosby Company.

The author of this monograph is Associate Professor of Medicine at Johns Hopkins University School of Medicine. The first edition was published in 1956 and new advances in the field of genetic disorders and in our understanding of connective tissue metabolism and diseases have necessitated an enlarged new edition with the text expanded by 130 pages and with the addition of over 80 illustrations.

The result is a completely up-to-date account of the Marfan syndrome, the Ehlers-Danlos syndrome, osteogenesis imperfecta, pseudoxanthoma elasticum and the Hurler syndrome. In addition, chapters are devoted to the clinical behaviour of hereditary syndromes, to the biology of normal connective tissue and to a variety of little understood disorders of collagen and bone, e.g. fibrodysplasia ossificans progressiva, osteopoikilosis and Leris pleonostosis.

The last decade has witnessed a tremendous surge of interest and research activity in the biology of the intercellular ground substances and connective tissues. The result is a vast literature but little enough in the way of a clear break-through. As the author states, the situation to-day is not unlike the elephant that was examined by 6 blind men. Nevertheless an enormous accumulation of data has been achieved and the serious worker in these fields will welcome this new compilation which has effected a useful synthesis of many scattered and diverse bits of information. Similarly, studies on the chemistry of heredity and the mechanisms whereby genetic aberrations exert their complex effect have shed much light on normal mechanisms and disease processes in general and detailed analysis of hereditary diseases such as is achieved in this volume is likely to prove of great value in solving the many problems of human biology.

DRUGS 1960–1961

Drugs of Choice 1960–1961. By Walter Modell, M.D. (1960. Pp. 958, including a complete drug index. £5 14s. 9d.). St. Louis: The C. V. Mosby Company.

This is a new edition of the volume published in 1958. It has 8 new chapters:

The Physical and Chemical Considerations in the Choice of Drugs;

The Choice of a Local Antiseptic;

The Choice of Drugs for Viral, Spirochaetal and Rickettsial Infections;

The Choice of Sedatives and Tranquilizers in General Medical Practice;

The Choice of an Anorexiant;

The Choice of Drugs in Endocrine Dysfunction;

The Choice of Drugs for Ophthalmic Use; and

The Choice of Drugs for Otolaryngologic Disorders.

In addition, it has a single inclusive Drug Index instead of separate lists of drugs for each chapter.

Most of the sections have been modified and brought up to date and the chapters on *The Choice of a Muscle Relaxant* and *The Choice of Drugs for the Treatment of Poisoning*, have been completely rewritten, the latter having been extended considerably. There is a useful elaboration of the section on principles in drug evaluation, and the new chapter on the use of sedatives and tranquilizers in general practice provides a helpful and concise summary of this confused field.

As in the previous volume, the method of approach to the textual matter is a valuable one, including as it does in most chapters, sections on *Clinical Applications, Pharmacological Considerations, The Several Drugs, A Design for the Use of These Drugs*, and the *Rational Basis for the Development of New Drugs*.

The general idea behind the compilation of this book, that of attempting to provide *expert opinions* on the selections of the best drugs for particular therapeutic problems, is very worthwhile, and there is a good coverage of the major areas of pharmacology and therapeutics.

It is intimated that the book will be revised and brought up to date at 2-year intervals.

SURGICAL ASPECTS OF MEDICINE

Surgical Aspects of Medicine. Edit. by H. Daintree Johnson, M.A., M.B., B.Chir., F.R.C.S. (1959. Pp. 382 + Index. With 18 Figs. 73s. Postage 1s. 9d.). London and Durban: Butterworth & Co. (Publishers) Ltd.

In this major work, edited by H. Daintree Johnson and contributed to by many of the leading surgical authorities, a complete coverage of all aspects of surgical practice in relation to the physician and general practitioner is undertaken.

The work discusses mainly the indications for operation and the results, and deals with some of the alternative techniques of surgical procedures. Late complications, prognosis and morbidity are discussed in full detail. It is interesting to note that in the chapter on upper gastro-intestinal haemorrhage, the plea is made for all such cases to be admitted under the care of the surgeon rather than the physician, so that early operative interference can be carried out rather than face a long delay under medical treatment.

Throughout this book the reader is introduced to and guided in the most modern form of surgical treatment. In the chapter on breast disease the basic principle in the approach of this difficult subject is in keeping with the teaching of the major British hospitals. In the chapter on the abdomen there is an excellent dissertation on pain in the right iliac fossa. There is also an interesting section on the pulmonary and cardiovascular systems.

This book is presented essentially as a guide for physicians and general practitioners in an endeavour to assist them in arriving at a decision about when

to refer the patient for surgical treatment. It is also an extremely useful addition in the armamentarium of the post-graduate student preparing for a higher degree.

GYNAECOLOGY

Synopsis of Gynecology. By Robert James Crossen, M.D., Daniel Winston Beacham, M.D. and Woodard Davis Beacham, M.D. 5th ed. (1959. Pp. 332+Index. With 106 Figs. 55s. 3d.). St. Louis: C. V. Mosby Company.

In this edition many chapters have been revised, new chapters added and a new approach introduced with the co-operation of the Drs. Beacham, who have joined the original author of the earlier editions.

This small handy book of 332 pages is printed on a glossy paper in an eminently suitable type and clearly illustrated, while the subject matter is broken up in each chapter under many sub-headings, a style which this reviewer finds helpful and which makes for easier study.

Senior medical students will find it an excellent book for quick revision of the more practical aspects of the subject—in particular the section dealing with the complete gynaecological examination; while the newly-qualified houseman will find it invaluable for quick reference.

The busy general practitioner will find in it, in concise form, a vast amount of useful information, ranging from anatomy and physiology to the diseases of the female pelvis, and including chapters making brief mention of medico-legal points, and the pre-marital examination, largely unknown here, but required by law, in varying degrees, in the United States of America.

Each chapter is followed by an extensive bibliography of selected references.

The 2 new chapters on endometriosis and on the complications of pregnancy, with discussions on abortion, hydatidiform mole and choriocarcinoma, are welcome additions.

PAEDIATRICS

Handbook of Pediatrics. By Henry K. Silver, M.D., C. Henry Kempe, M.D. and Henry B. Bruyn, M.D. 3rd ed., 1959. (Pp. 572 + Index. With 20 Figs. 29s. 9d.). Los Altos, California: Lange Medical Publications.

This *Handbook,* now in its third edition, should have a strong appeal as a paediatric *vade mecum* to medical students, interns, registrars, and general practitioners. It is a concise digest of established concepts of paediatric disorders, their aetiology, clinical findings, complications, prophylaxis, prognosis and treatment.

The *Handbook* is not intended to replace standard textbooks with references to paediatric literature. The authors are top-ranking paediatricians. Drs. Silver and Kempe are Professors of Pediatrics, University of Colorado School of Medicine, Denver, Colorado. Dr. Bruyn is Associate Professor of Pediatrics and Medicine, University of California School of Medicine, San Francisco, California. Such distinguished authorship lends to the *Handbook* a stamp of authority. It is packed with facts and figures pertaining to every phase of paediatrics—*multum in parvo.*

The *Handbook* fits readily into the pocket or medical bag. The format is attractive. It is an excellent book for the purpose stated.

CORRESPONDENCE

PROPRIETARY PREPARATIONS: INCOMPATIBILITY OF MIXTURES

To the Editor: With the ever-increasing volume of new proprietary pharmaceutical products appearing on the market, many containing only one active ingredient, there is a natural tendency for prescribers to wish to use a mixture of two or more liquid preparations or to prescribe the addition of other drugs to a marketed formulation in order to provide modifications in action, additional therapeutic effects or the avoidance of side-effects. Questions on the compatibility of mixtures of certain pharmaceutical products are often referred to pharmaceutical manufacturing companies, who alone are aware of the nature of all the materials included in the formulation and of the factors governing their stability. In many cases, however, admixtures are prescribed with perhaps little more than a cursory consideration of the possibility of incompatibility, which may result in rapid loss of potency or precipitation of one or more active ingredients.

The maintenance of an optimal pH is essential for the stability of solutions of some drugs, e.g. vitamins of the B complex and certain antibiotics, and the alteration of pH by mixing the solution with other preparations or by adding a further drug may result in rapid loss of potency, especially on storage at adverse temperatures. Changes of hydrogen ion concentration can also result in precipitation of drugs from solution, the addition of such mildly acidic substances as alkaloidal salts serving to precipitate theophylline from many of its soluble complexes or barbiturates from solutions of their alkali metal derivatives. Changes in solvent caused by admixture can also affect the stability of liquid formulations, as when alcoholic solutions of one or more organic bases are diluted with a preparation of which the vehicle is aqueous.

The effect of additional aids to formulation in one preparation, e.g. stabilizing agents, solubilizing agents, preservatives, colourings and flavourings, on the stability and potency of a second preparation, are much less predictable and may even be unknown unless specific stability tests are undertaken. There would, however, be good grounds for suspecting that a reducing agent added to stabilize one product could well have a most adverse effect on the potency of the drug contained in a second product, and that solubilizing agents, whether anionic, cationic or non-ionic, could result in wide-spread antagonism of many drugs included in other preparations.

In view of these risks which attend the prescribing of combinations of proprietary pharmaceutical liquid preparations, it would obviously be a wise precaution to employ separate administration of two or more preparations and not to mix proprietary preparations in any circumstances.

B. A. Wills,
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